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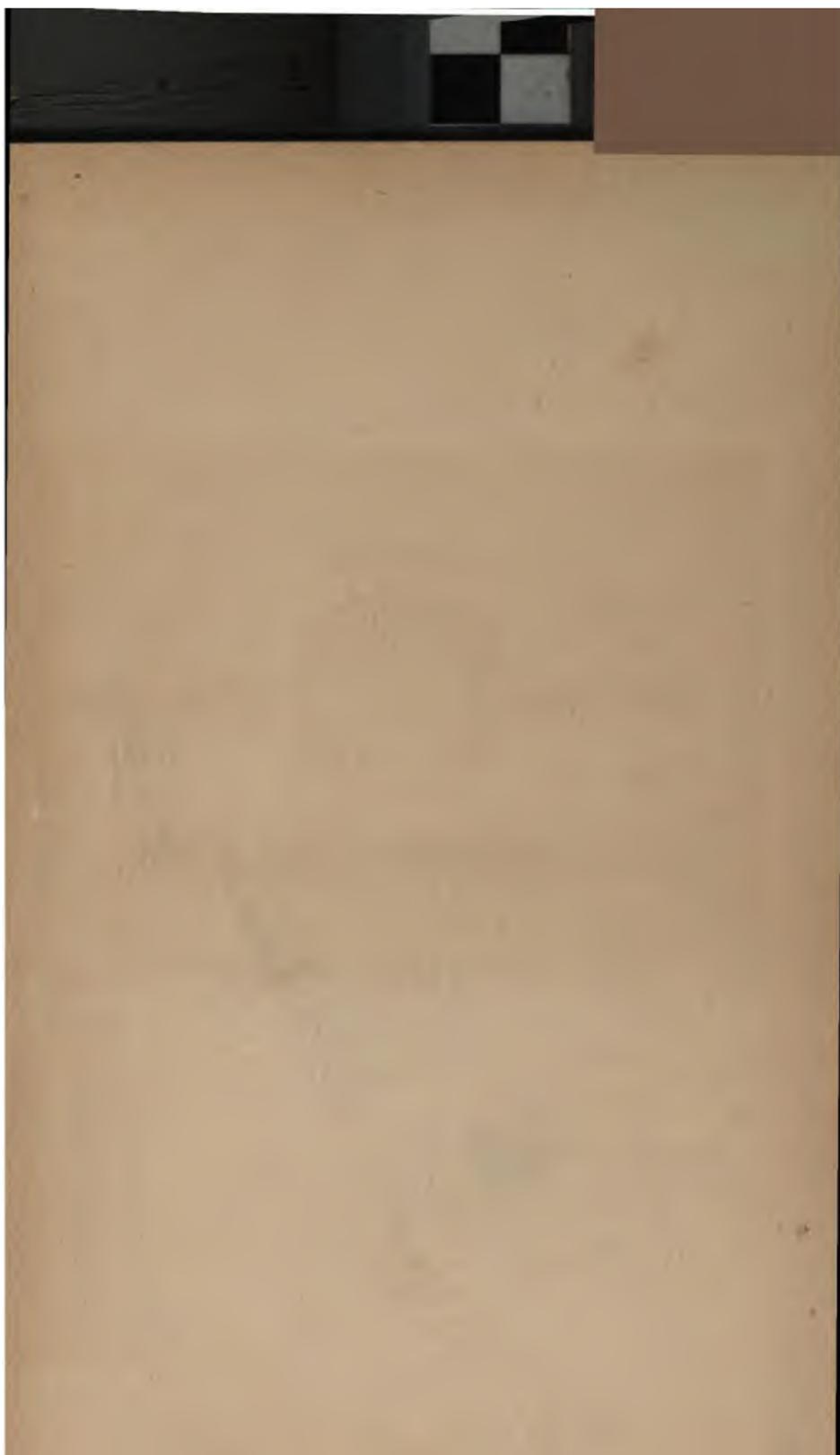
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O. Rosenkranz.

PHYSICIAN
VERSUS
BACTERIOLOGIST

BY
PROF. DR. O. ROSENBACH

OF BERLIN

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Authorised Translation from the German

BY
DR. ACHILLES ROSE

THE truth should be constantly repeated, because error all around us is preached again and again, and not only by the individual, but by the masses. In newspapers and encyclopedias, in schools and universities, everywhere error has the upper hand, and it feels happy and comfortable in knowing that the majority is ranged on its side.

—Gullé.

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Dr. John W. Brown
1850

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—Goethe.

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PREFACE

THE desire of a number of my friends—and, I may add, my own—to present in one volume my discussions on bacteriologico-clinical and hygienic problems to the profession at large, has, for important reasons, remained unsatisfied for a considerable length of time. This was not due to the fact that I feared to be charged with self-adulation for attempting, at this so very productive and rapidly changing period, to resurrect as being of unusual importance certain investigations, the original publication of which in part dates back more than a decade; nor was it because I dreaded the reproach of unscientific obstinacy which, in contrast to the belief of the overwhelming majority, persists in preconceived opinions. I was guided, above all, by the trivial notion that truth was bound to prevail in the end, and that then those men would be remembered who, fully aware of the thankless task of restraining Utopian hopes, have devoted a considerable share of their energy and love of work to battle against the overgrowth of bacteriology, and who have emphatically pointed out to overzealous enthusiasts that the doctrines of orthodox bacteriology, far from solving even one of the enigmas of medicine, on the contrary render the comprehension of clinical processes more difficult, and, above all, are fraught with serious dangers in a social as well as in an ethical aspect.

But the objections to the publication of this collection

have all been removed in view of the change which has taken place in the course of the last few years, and which is the less to be mistaken the more the supporters of bacteriological doctrines persist in sounding their victorious shouts. In fact, according to our opinion, the exclusive laboratory bacteriologists—who, by reason of an unjustified equalization of experimental injection disease with clinical infectious disease, usurp not only the domain of etiology but also the entire realm of pathology and therapy, a domain, therefore, which is naturally closed to them because it is accessible only to the most experienced physician—have, in view of the force of facts, been driven already to a state of defense. Instead of a violent onslaught we observe nothing but retreat, which often is arduously concealed; to keener minds its distinct signs are the drastic shifting of the mooted problems. The original dogmas, compared with the present ones, are practically nothing but the abandoned outposts of an aggressor who, by the force of facts, is gradually compelled to defend his original possessions.

This struggle once more confirms the old experience that positions which at the outset were most actively acquired as the reward of victory, are finally represented as unimportant and as never being actually coveted if the impetus of the attack enforces their abandonment. That means in our case: Whereas formerly the exclusive bacteriologists considered the microbes to be *everything* and did *not concede anything* to predisposition, individuality, etc., now the most radical hotspurs maintain that nobody ever doubted the significance of external and internal influences. However, this admission means the same change regarding the fundamental problem as was ushered in in antimicrobial therapy with the transition

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from antisepsis to asepsis, or, in the realm of history, with the scrutiny of formerly accepted records.

This shifting of problems naturally tends to obscure the true character of the controversy and with it the true state of affairs; therefore, to prevent this obscuration I publish once more—with some abbreviations and a few unessential alterations in style—those essays which, closely connected, will demonstrate the real object of the controversy to the unbiased reader, and show him the principal shifting of view-points which has taken place in the last few years. It certainly appears *a priori* unlikely that persons with fairly good common sense, simply for the sake of sport or moved by a spirit of contradiction, should have devoted so much valuable time and irretrievable energy to contest what is obvious or to prove what is not disputed—*i.e.*, from the love of combat to create unnecessary objections and to embitter the enjoyment of scientific progress. But one who does not retrace his steps to the original sources will never become aware of the gradual transformation of dogmas, of the imperceptible exchange of view-points; and hence this collection purports to furnish to the impartial observer, and possibly also to the future historian, objective material wherewith to judge the contention, the contenders, and the form of contention.

To eliminate all doubt as to my position regarding the past verdict in the case of “physician *versus* bacteriologist,” I must state that I do not consider the same as not being subject to appeal, and for this reason I have purposely chosen a title which may not enlist the sympathies of all, but which, in my opinion, clearly defines the situation. Now that an unquestionable change of view-points, and hence of the scientific points at issue, has

taken place, I once more present for unbiased consideration those evidences which are characteristic of the various stages of the controversy. And not only those which the physician, endangered in his possessions, is justified in bringing forward to secure his rights, in opposition to the demands of the bacteriologists (who dare to direct the course of this world from their official table and to ignore well-established facts), but also proofs of the social and ethical dangers which would arise from an absolute supremacy of bacteriology.¹ More particularly have I fought against bacteriologists operating *in absentia*, a court council of war, as it were, who, remote from the raging battle, consider themselves capable of giving directions to the real fighters in the battle against disease. On the other hand, bacteriology as a biological science, concerning itself with qualities of smallest organisms, can not be too much promoted. It is capable of far-reaching development. As I have stated at other times, especially will the study of symbiotic processes yield manifold disclosures in physiology, altho its importance regarding the origin of disease may have been greatly exaggerated. The strictly scientific problems, therefore, important as they are, do not appear to me to be the main object of the controversy. The principal interest centers in those unpleasant consequences to physicians and to men engaged in the broader fields of social and ethical activity which result from the predominance of one-sided bacteriological thought. I

¹ To avoid being accused of seeing things in their darkest aspect, let me quote the language used by Martius in his excellent work, "Pathogenesis of Internal Diseases," concerning my explanations in regard to this subject. He says: "It is the merit of Rosenbach that years ago, at a time of bacteriological high-tide, he pointed out, with great acumen and with moral courage, the inhuman, antisocial, and, in fact, actually unchristian consequences that were bound to develop from this view."

do not hesitate, even to-day when the heat of battle has passed, to state the opinion that nothing has so injured the standing of the practitioner and of the medical profession as the eagerness of bacteriologists to transfer decisions from the bedside to the laboratory, and to regulate etiology, diagnosis and therapy, endemics and epidemics, individual and general prophylaxis, according to an artificial scheme, instead of making full allowance for the requirements of actual conditions which can only be judged by those who are present at the bedside and who are familiar with local conditions. Finally, I am now compelled, as I have done formerly, to hold the encroachments of the "nothing-but-bacteriologists" responsible for the deterioration of important ethical principles. The advent of fear of infection has transformed the love for the patient into fear of the patient, as in the days when disease was looked upon as the working of mysterious demons and the patient as an enemy of divinity and of man. If we seek for the exclusive cause of disease and pest in a so-called source of infection, instead of in general and individual effective conditions—among which microbe activity plays a comparatively unimportant part—we shall most naturally arrive at a complete misjudgment of the significance and manifoldness of causes of disease, of the nature of epidemics, and of the part played by social and hygienic factors. Hygiene, the science of prevention of disturbances of function, then resolves itself into a manipulation of disinfectants. But if the patient, as the tangible focus of infection, is in reality the only cause for infectious diseases, which I deny, the question arises: Is fear of the patient and the logically deducted necessity of ever excluding from intercourse with mankind more and more patients as

sources of contagion at all humane? Quite apart from the fact, according to my experience, that association with the sick, and especially with mild cases, promotes protection against infection, should we not consider the consequences which must naturally follow upon openly avowed fear in times of epidemics, and the responsibility which is placed upon those who disseminate as scientific the opinion that a sick individual is able to spread an epidemic, and that the physician or sanitary officer who has neglected certain requirements (hatched out by Utopian theorists, but impossible of fulfilment in practice) relating to the diagnosis of the so-called first case, or regarding prohibitive measures, lays bare a city or even an entire country to a disease, like a traitor who knowingly opens the gate of a fortress to the enemy? Is it at all conceivable, furthermore, that self-sacrificing, courageous physicians can still be educated when infectious patients are made accessible to the embryo physician only through glass windows or steel bars, like wild beasts? What is left of the safety vouchsafed by much-lauded vaccination if even vaccinated students are not allowed to come in contact with smallpox patients? How little was wanting at one time and compulsory inoculation of the tuberculous or for diagnostic purposes would have been introduced by law!

From what point dates the decline of the standing of the practitioner unless from the time of the domination of the bacteriologists who have achieved that the diagnosis becomes subject to the infallible arbitrament of the microbe cultivator remote from the bedside, and that the physician submissively bows even in therapy to the specific means discovered from time to time?

Therefore, I believe that I am fulfilling a duty in col-

PREFACE

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lating my discourses despite, and just on account of, the doleful experiences through which I have passed in this controversy, not by refutation of my reasons, but by imputations, by doubts as to my right to criticize, and still more by disdainful silence. But the number of critical medical examiners is growing, and it is a source of satisfaction to me that many a one has drawn his inspiration for independent observation from my discourses. No reader will probably refuse to acknowledge that, uninfluenced by the fascinating opinion of the day, I have endeavored to discuss difficult problems from actual experience and in as many different lights as possible—i.e., with incisive criticism, but objectively withal. The future will decide whether I am right or wrong, and in what respect I have gone too far: *Post fata nostra pueri, qui nunc ludunt, nostri judices erunt.*



TRANSLATOR'S PREFACE

THE history of science tells us of many disputes between the representatives of opposing opinions—disputes of far-reaching consequences. Some of these controversies have ended with the discovery that the truth does not lie on either side ; indeed, many of the historical disputes which have been conducted most seriously now serve only to excite hilarity.

It is a grave matter when a mere hypothesis is forced into the position of a dogma, adopted as infallible, and made to rule the daily actions of life, and especially when, under such circumstances, men of learning become adherents of erroneous teaching, lose their common-sense judgment, and act in obedience to the lucubrations of some "authority" of the day.

The majority of mankind will readily believe in eccentricities when they are pronounced *ex cathedra* by some one who is recognized as the discoverer of a new truth.

The astonishing results of experimental researches of exact investigation in the field of natural science have developed a respect without bounds for teachings based on such researches.

The reign of theory in medicine has rarely been stronger than during the last two decades, because this Utopian reign found protection under the cloak of the alleged infallibility of the laboratory experimentation.

The truth is, that many have overlooked the fact that experiment is of value only under certain conditions, and

that its results must not be generalized by means of hasty deductions promulgated with artful dialectic.

I have undertaken the translation of Rosenbach's book, "Arzt contra Bakteriologe," into English, in order that my English-speaking colleagues may learn what this independent and original investigator has said on the great problems of medicine of to-day, and what he has written to restore the rights and reestablish the position of the general practitioner, which have been encroached upon by a morbid proliferation of specialism and a one-sided organotherapy.

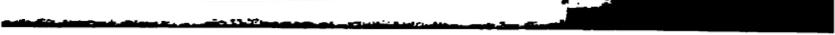
The reader will see that Rosenbach appreciates fully the value of bacteriology as a biological science, the importance of the study of the microscopical world; he is well aware what surprising biological information and what important methods are to be found in the study of bacteriology, but he raises his voice against the unjustified, the unwarranted claims of the bacteriologists, especially of those whom he calls "nothing-but-bacteriologists," the diagnosticians *in absentia*, with their disinfectants and measures based on unsupported theory. This shaft is aimed at tuberculin and the legion of serums.

The bacteriologists, by means of fallacious conclusions, have established—in opposition to all common sense—the dogma that all infectious diseases are caused by bacteria, and that all diseases in which so-called specific bacteria are found are infectious diseases. Since this unsubstantiated teaching has become so popular that it is matter of common comment in the daily press, and all the world is thus driven to really dangerous bacteriophobia, it is certainly opportune to have Rosenbach's views on such aberrations.

A. ROSE,



PHYSICIAN
VERSUS
BACTERIOLOGIST



I.

ON THE MUTATIONS OF THERAPEUTIC METHODS, WITH SPECIAL CONSIDERATION OF THE DOCTRINE OF ANTISEPSIS¹

*Mutations of Therapeutic Methods—The Law of Contrasts—
From Antisepsis to Asepsis—Antisepsis in Internal Medi-
cine and the Combating of Infectious Diseases by Para-
siticidal Agents*

THE history of medicine teaches that any and every method of treatment has always been *followed by a method based on exactly opposite principles*; it further demonstrates that all these contrasts have been upheld by their fanatic adherents with the same fervor and under cover of equally unassailable statistics, so that, as a matter of fact, *every form of treatment*, at least in the opinion of its chief supporters, may justly claim identical value as to efficacy and healing virtues. It follows, since it would be unreasonable to ascribe identical efficacy to all therapeutic efforts resulting from opposing views and usually sharply contrasting to methods in vogue, that none of these superlatively praised systems may possibly have been effective in pathological processes in which they were applied. This conclusion is strengthened by the well-known fact that every new method is vigorously attacked at its *début*, and later on, having once acquired followers among former opponents, is praised as infalli-

¹ "Grundlagen, Aufgaben und Grenzen der Therapie" [Foundations, Problems and Limits of Therapeutics], pp. 3-9. Vienna and Leipzig, 1891.

ble, the most astonishing therapeutic results being ascribed to it, until subsequently, while it is still in the lime-light of apparent success, doubts are cast upon it, and it is finally, with the same enthusiasm, supplanted by a new method which, according to *the laws of contrast*, is the opposite of its predecessor.

Why do we drop methods so safely anchored in favorable results? Why may one prophesy, with no chance of missing it since the prediction is based upon the history of therapeutic fashions and mistakes, that this change is bound to come, and what particular course it will follow? Simply because *these lines of treatment are not the result of the application of truly scientific principles obtained by observation at the bedside*, but are simply the *expression of certain results of laboratory investigations*, now becoming quite popular, the practical expression of a precipitate of catchwords calculated to generalize a certain view-point of physical or biological perception for the benefit of non-observers—a differentiation necessary to uphold as agreeable to the purpose. Considering the relatively small satisfaction furnished by the final results of his therapy to the physician of average critical tendencies, not only the yearning for new remedies is ever active—this is most naturally and strikingly manifested in the chase after new remedial agents—but, stimulated by his desire to search for the causes, and aided by a consciousness of his position as an apostle of natural sciences, he will become possessed of a wish to have his therapeutic action firmly founded on a scientific basis. Therefore, becoming convinced that his past and present methods show imperfect results from a practical standpoint, the physician will speedily become inclined to look upon the foundations of his activity as false and

insecure, and to regard a modern conception—one that arrogates to itself the standpoint of most recent knowledge—as all the more infallible, the stronger is its contrast to the former one, now appearing antiquated and altogether false. A new conception, therefore, if this contrast is very conspicuous, will at once be accepted by a large percentage of physicians, because the old idea has been recognized by practical experience to be insufficient. However, the other contingent of conservative tendencies, ever satisfied with present conditions, will fight it no less for its clearly apparent improbabilities than because it relegates the old system to oblivion. As of old, the more formidable the attack, the more certain is it to excite attention, and, in accordance with the *law of contrasts*, this will only serve to prepare acceptance and instillation of the new ideas into the minds of those whose brains have become sluggish through following prevailing conceptions, and on whom, therefore, nothing short of a contrary opinion exercises a strong charm. Would the Darwinian theory ever have gained one-half of its popularity had not powerful opposition been aroused by its clever, if false, deduction of the descent of man from the monkey, and thus excited the attention even of sluggish minds and of the laity? Did it not, by this *clever clap-trap*, offer a premium to many to proclaim themselves freethinkers and modern observers? *The psychological law of contrasting effects which teaches that a brain, dulled to a certain extent by constantly acting lines of thought, is made the more pliable and receptive for new theories—after a period of reaction to them—the more divergent they are from the old.* This true psychological law, which is based upon the physiological law, that variety is the spice of life and the *only remedy for the tired and mentally be-*

numbered, while simultaneously acting as a *double incentive for renewed activity*,¹ is of greatest importance to the therapeutic views of the physician as well as of the layman, inasmuch as all therapeutic fashions, after all, depend upon it just as much as do all visible processes of daily routine denoted by the term "fashions," which, sometimes quite suddenly, sometimes after a period of preparation, relieve each other with greatest regularity.

A retrospective glance at some of the most prominent therapeutic methods, each in its time received with

¹ The effect of the action of contrasts upon the brain may be conceived, in analogy to the processes of bodily stimulations, as follows: If the circle of conceptions of a certain individual has not become widened in the course of a long period of time by new impressions, the faculty of the mind to create new combinations of thought gradually declines, as psychical activity moves only in the accustomed tracks. Since increased function by practise is nothing but the occupation of an organ by new, successively growing stimulations which increase irritability and, owing to stimulated nutrition, increase also the work performed, and, further, since the decrease of activity of an organ is identical with a diminution of its irritability (capability of stimulation), it follows that, in a brain thus constituted, *conceptions will act as a stimulation only when they are not alone new, but also when they are as much as possible in contrast to those that were prevalent until then.* They act as a stimulation—*i.e.*, they excite attention, they are observed, they combat prevailing conceptions—*i.e.*, they are compared with them—and by this form of association they soon obtain not only the same importance as the older ones, but they gradually displace them entirely as *more powerful stimulations*—which in turn will become subject to the same fate. Owing to the average quality of the brains affected thereby, this psychical process requires for its successful operation nothing but a contrast of conceptions that is as striking as possible, as only such can act as a stimulant in a moderate irritability of the brain—*i.e.*, can command attention and, at the same time, contradiction (immediate comparison to former combinations and sensations of dissatisfaction caused thereby). This new view, furthermore, to be markedly effective, necessarily must impress itself easily upon memory by means of a symbol (catchword), for the average brain is capable of connecting a line of thought only with something tangible. Hence the accumulation of catchwords in place of the development of sound logical deductions.

The striving for action is manifest in the intuitive requirements of the brain for new stimulations and conceptions called forth by the organs of sense. Fashion with its contrasts—be they mental or bodily fashion, fashions of the manner of thought or of garment—therefore promulgates only the tendency of the brain to manifest that function which, in the majority of men, is nothing but a receptive, not associative one: the prevention of mental lassitude and stability.

unbounded enthusiasm, will show that what was looked upon by so many of the profession as the symbol and nature of true therapy, was too frequently naught but arabesques, in which *a minimum of content is obscured and made to appear large by a mass of filigree work foreign to the substance*, serving only to veil the kernel in the center. We shall soon become convinced that certain complicated formulæ which throw a halo around certain methods, if for no other reason than because they are allegedly mastered in their entirety only by the initiated—it might be in place to call them, in contrast to specialists of a certain realm, *specialists of a method of treatment*—are nothing but superficialities, serving as a basis to minds that adhere to catchwords and formulæ. It will further be noted that, in a number of therapeutic methods which have readily acquired citizenship under the flag of a scientific foundation, *the scientific premises are either entirely untenable or, to say the least, are not by any means proved nor capable of demonstration*. However, we shall also prove that, in many scientific truths which did not create sufficient impressions solely on account of their simplicity and obviousness, such extraneous ornaments were necessary to command general attention, and that the simple, yet significant, kernel could be taken from the shell only after its inherent value had been demonstrated in a foreign guise.

Let us begin with a method which has stamped its trade-mark upon the new era, and under the auspices of which surgery achieved its greatest triumphs—namely, antiseptis. Who fails to recall the fanaticism which, in the beginning of the new era, proclaimed every detail of the method as absolutely indispensable to the success of operations? Who at the time would have dared to think

that the antiseptic spray, the drenching of the wound surface with the most concentrated antiseptic drugs, the handling of tissues with various chemicals, the continuous covering of wounds with carbolic acid lint, the most complicated bandages—all were *entirely foreign to the real spirit of the method*, that they were nothing but a mass of details, confused attempts to employ a true principle, the real nature of which has not been yet recognized, with the exaggerated application of theoretical maxims?

What remains of all these details at the present day? Not unlike the alchemist who, setting aside and ignoring nature's methods, could or would not arrive at the simplest deductions without the aid of the queerest and most complicated, often superstitious, measures, until, setting out from correct, lucid premises, it became known how to separate the essential from the unessential, so did antiseptics proceed on its road to *asepsis*. Those who then made light of carbolic acid and the spray, and were decried as heretics because they saw dangers in the insults offered to tissues in the toilet of the peritoneum, the reckless lavage of the uterus and of the pleura, because they could not be convinced that antiseptic solutions of varying degrees of concentration would destroy germs of infection in tissue already infected—this minority of skeptics have lived to see that no antiseptic remedy is considered any longer as the only efficacious one. They will note that the spray is abolished, that the toilet of the peritoneum is voted harmful, and that washing out of the pleura is reduced to a minimum. With satisfaction, not unmixed with pain at the former mistakes made by the fanatics of antiseptics, the skeptics observe that poisonous antiseptics are now used in small quan-

tities and brought into contact with tissues in selected cases only; this because the conclusion has been arrived at that many cases of death and complications in confinements and in surgical operations are not due to the actions of nature, of the fight of carriers of infection with the body, but to the deleterious by-effects of antiseptics. The time is not far off when antiseptics will, in most cases, be used only for disinfecting the external skin and the instruments. Water and soap will be reinstated in their place of honor as cleansing material. The quintessence of antiseptics, as explained long since by many successful operators whose work is done without the aid of bactericides—which, in truth, had better be called tissue destroyers or protoplasm poisons—will be reduced to an endeavor to avoid the introduction of additional virulent agents into the human organism by our operative measures (which must in part destroy the protective barriers of the organism, owing to the necessity of entering the interior of the body); therefore, to operate with clean hands, clean skin, and clean instruments, as well as, above all, to handle or squeeze tissues as little as possible, in order not to reduce their defensive apparatus by local necrosis, and thus to assist in facilitating the process of regeneration. That all this may be accomplished by the simplest means of relief, provided *practise and dexterity* are in evidence, reducing the insults to a minimum, is illustrated by the history of ovariectomy.¹ That not all operations can be rendered harmless goes without saying. Likewise that, in spite of all precautions, a certain percentage of unfavorable results do now and will ever occur. We do not deny that this

¹ This is a hybrid word. The correct Greek term is "*Oothecotomy*."—THE TRANSLATOR.

number may be reduced to a minimum by careful attention, but we hold that, even after a most scrupulous exclusion of all disastrous possibilities, other difficulties will present themselves which will remove to the distant future any possibility of curing patients *cito, tuto et jucunde*. If the yardstick of absolute safety from infection be applied to our operative proceedings, it would be clearly impossible ever to find an operative method that would guarantee such success. There is always the possibility, with our present means of disinfection of the operating-room, that a microbe from the atmosphere may again infect the previously disinfected knife, the hand of the operator, or some portion of the tissues involved. But complete disinfection is not requisite, since germs do not float in quiescent air in such enormous quantities. Above all, it should be remembered that tissue as yet untorn and unsqueezed possesses sufficient means of defense of its own to eliminate the relatively limited number of germs. Hemorrhage alone limits this invasion both mechanically and biologically. Small numbers of infectious germs are either incapable of working mischief when in contact with a bleeding surface, or else, entering tissues that were not destroyed by the knife or by antiseptic agents, are rendered harmless in the tissues themselves. Not to speak of the expense, etc., of such a method, if killing of germs were aimed at to the extent of their total destruction within the purlieu of operator and assistants, the atmosphere of the room would be so filled with poisonous substances that the effects would manifest themselves on the patient, physicians, and nurses. To make the scientific postulate of absolute freedom from infectuous germs available in the field of practical medicine is altogether an idle dream.

The fact that well-cleansed hands dipped into nutritive gelatin carry germs, as shown by the ready cultivation of these in artificial media, does not prove that the same cleansed hands will ever be able to produce inoculation in the human body, which is not a culture ground, nor yet to infect a wound surface. An operator who works gently and deftly and does not imagine that, under cover of strict antiseptics, any and every abuse of tissue is licensed, will always command brilliant results. The dogma of the efficacy of *purely external* disinfection being such absolute protection as to render superfluous any regard for the patient, or the healing powers of nature, has been provocative of more mischief than the adherents of absolute protection by means of toxic antiseptics will ever care to acknowledge. In the battle of bacteria with tissue cells, the weaker will be conquered; antiseptics introduced into the body kill the finely organized cells of a highly organized being, or, to say the least, minimize their powers of resistance more quickly than they similarly affect all micro-organisms.

Several years ago *internal medicine* seemed destined to experience a brilliant revival in therapeutics. Based upon confidence gained in the surgical field by the supposed success of antiseptic methods, salvation was sought for in parasiticidal remedies of high potency. The fact that previous results were founded upon asepsis was for the time obscured. Without hesitancy, the apparently telling consequences of antibacterial methods were carried over into the domain of infectious diseases, and the search for microbe-destroying antiseptics began, with results that only forced upon us the conviction that, in spite of all beautiful theories, remedies which have achieved brilliant results in the laboratory not only

prove ineffective in therapeutics, but are positively harmful. Part of these causes may be gleaned from what was dwelt on above. Another reason was, as shown by the investigations of Pasteur, Brieger, and others, that not the bacteria but the *toxins produced by them were the cause of disturbances in the human organism.*¹ Since, naturally, the attempt to paralyze the activity of ptomaines by anti-parasite remedies is without result, since it is difficult to guide these remedial agents in proper concentration to localities in which microbes have infested tissues, it becomes evident that true *internal antiseptis*—if it be permissible to use this term also for the faculty of arresting the development of bacteria—is only to be thought of under very exceptional circumstances—namely, when the microbes produce relatively harmless substances, and consequently do not harm tissues by sustained intensity or permanency, when their vital energy is not potential so as to admit of being influenced by remedies of moderate concentration, and, finally, when microbes are found in localities quite accessible to remedial agents.

All attempts to square laboratory results with the actual conditions of war between organic cells (bacteria and animal cells) are void of result. The resisting powers of the invaded organisms can not be reduced to

¹ Allowing that the toxins are concerned in the manifestations of disease, it must not be forgotten that bacteria play an important part in all diseases, since in every case they exercise locally mechanical actions, and since, above all, they are the constant producers of toxins which, should it even be possible to limit for the time being the toxins then in active service, would render necessary constant warfare between remedies and toxins, just so long as the bacteria themselves—the generators of the disturbances—are not rendered harmless. It follows that, in operating from a therapeutic and not a hygienico-prophylactic view-point, persistent endeavor is required to find remedies that are parasitocidal in the sense not of their killing microbes by direct contact—for this is impossible—but of their making the conditions of existence for these germs as unfavorable as possible.

figures, inasmuch as the artificial culture grounds used for test-tube experiments, unlike the tissues of the body, are always of uniform quality, and therefore require a disproportionately greater potency of those remedies intended to arrest development. All laboratory experiments serve only *to show life and extent of the formation of minute organisms, entirely undisturbed by any "living" agency, and to reveal the unquestioned fatal effect upon protoplasm of added chemical or other agencies.* Thus it has been demonstrated by experiment upon artificial culture grounds that this soil is exhausted in the course of time. From the fact that at a certain concentration of products in alcohol fermentation the increase of yeast is arrested, it was also assumed that the accumulation of certain products of tissue metamorphosis of microbes in the end proves fatal to the latter. Both facts are of record, but their application to observations in the human organism is viciously false. *The human organism is not a limited nutritive ground in the experimental sense.*

Ever active tissue metamorphosis brings continuously fresh nutrient material, unless, which is rarely the case, the morbid areas are eliminated from the circulation, and in the usual manner cut off from vascular supply and from the lymphatic system. *However, this same metamorphosis is quite as likely—not always to the advantage of the affected individual—to carry the products of bacteria to neighboring cells and to distant organs, so that an accumulation of toxins and a choking of the microbes "in their own fat" appears out of the question.* This contact of toxins with healthy cells is precisely the cause of reaction, putting these cells into a condition of intensified irritability and tissue activity, and thus presenting to the microbes a most favorable soil, in the true sense

of the word, through the abundant supply of nutrient fluids. In the development of this reaction in the struggle for existence certain advantages for the organism are not excluded—ample supply of “defensive proteids,” rapid combustion, and elimination. But be it remembered that the extent and manner of these processes, and their relation to the defensive efforts, have not been so fully established as to base upon them a safe system of therapeutics.

The possibility of certain substances shielding, or at least assisting, the attacked animal organism is by no means excluded. On the contrary, that they can do so and why are clearly shown above. *They must be capable of being absorbed by the living cell, thereby increasing its power of resistance.* They must remain in the body so long as the inimical agency is still active, and must, therefore, be supplied, not irregularly, at any period, but as nearly as possible at periods corresponding to the activity of the foreign agent. Such remedies must be of *weak concentration, so as not to paralyze the activity of the living cell,* while at the same time they aid in shielding it against renewed attacks of foreign cells by making untenable the vital conditions necessary for the activity of these assailants.

II

SIGNIFICANCE OF ANIMAL EXPERIMENTS FOR PATHOLOGY AND THERAPY—INJECTION DISEASE AND INFECTIOUS DISEASE¹

FAR be it from me to deny the importance of simple, uncomplicated animal experiments in a series of questions concerning the function of a certain animal organism. Much as I acknowledge the value of operative and exploratory proceedings in establishing correct views as to the functional capacity of various organs—I need only mention extirpation of the pancreas—it is well to keep in mind the limits of these methods of observation, and not to be persuaded that in the majority of these cases the test conditions in an experiment ever so carefully conducted may in any wise imitate or be a substitute for slowly progressive changes manifested by disturbances of function which are called disease. Hence, even a mild experimental lesion can present only the maximum of compensating activity, never the sum total of those minimal compensating contrivances possessed by the organism.

We have neither exact nor definite methods of testing these mild but none the less important functional changes, nor do we possess remedial agencies to make our experimental interferences so insignificant that the whole compensating capacity of the organism may be

¹ "Grundlagen, Aufgaben und Grenzen der Therapie" [Foundations, Problems and Limits of Therapeutics], pp. 21-25, 54-55. Vienna and Leipzig, 1891.

called into action. Neither do we possess a criterion for judging whether or not an animal responds with full compensation in spite of the invasion. In previous publications (Virchow's Archiv, vol. 105) I have pointed out that unchanged blood pressure, either during or after an experiment, does not at all prove that full compensation has taken place—quite apart from those lesser variations in pressure that, after all, represent for the organism a considerable change of vital conditions, altho not made manifest by our methods. Thus it would be obligatory to establish fulness of blood vessels, rapidity of circulation, the behavior of the vasomotor apparatus, secretion of glands, and absorption at one and the same time, and to determine that the same conditions existed previous to the interference before we could be justified in assuming an exact compensation for the created lesion.

Tho the changes found to be present are seemingly so insignificant that they can not be determined by our imperfect methods (as little as can the manifestations of reaction in the body), it does not prove that we are dealing with inconsequential matters; for let it be remembered that in the continuity of animal life every irritation, even the very smallest changes, will in the sum total represent high potencies. Consider what extra work is put upon the heart muscle when the blood pressure, with pulse at 100 to the minute, rises by the apparently small difference of 1-10 mm Hg. Yet this represents a blood pressure elevation of 14.4 meters in twenty-four hours, and is in accord with the rule: "Small causes, great effects"—a truth in experimental investigations quite too frequently overlooked.

Experiments can give us facts only on certain terminal points. Only under rare conditions true light may be shed upon more intimate changes that occur during the

course of disease in any organ. Even in cases in which the issue and the operative procedure are comparatively simple, the result can not be generalized and be transferred from one animal species to the other, least of all to man.

Setting aside a few infectious diseases, such as anthrax, acute miliary tuberculosis, and tetanus, we have not succeeded in creating disease in animals truly identical with disease processes in man. But even in the above-named diseases some important questions concerning the difference of the material and the difference of the infection, especially in a quantitative sense, are still unsolved because they have been decided too much in a one-sided manner, solely from the results of the animal experiment. Even here the conception of experimental injection disease is by no means congruent, as some investigators maintain, to an infectious disease that has arisen in a quasi-natural manner.

In tuberculosis, for instance, experimental researches have only shown, according to our opinion, that acute miliary tuberculosis is unquestionably caused by bacillary infection; but concerning the part that the tubercle bacillus plays in so-called phthisis, we are by no means enlightened. Indeed, it seems as if the exclusive acceptance of bacillary etiology may have led us away from the true path of solving these problems; for, in view of the mere *possibility* of infection, we are beginning to underrate the significance of individual disposition and of the part played by already existing lung diseases, inflammations, and catarrhs, notwithstanding the fact that clinical experience daily demonstrates the importance of these factors. The simple fact, even, that this bacillus occurs everywhere, and that hap-

pily the disease is still relatively rare, added to the experience that, notwithstanding the undoubted presence of disease germs in rooms inhabited by human beings, certain simple hygienic measures (that do not even require the absolute death of germs in the sputum), and, above all, absence of hereditary tendencies, protect from infection in the majority of cases; further, that the mucous membranes of mouth, nose, and conjunctivæ are comparatively rarely affected; finally, the consideration of effects produced in all tissues by suppurative and inflammatory microbes in the inception and progress of phthisis should keep us from overestimating the influence of the tubercle bacillus. It appears to us, after numerous investigations along diagnostic lines also, that the exclusive stress laid upon the importance of the tubercle bacillus, which we do not by any means under-rate, is going a little too far, for, according to our experience, it is quite doubtful whether in pure tuberculosis of the bronchi, of the larynx, and of the pharynx, showing merely a tendency to form nodules, with a termination in uncomplicated cases of fibrous consolidation or caseation, bacilli were ever found in the sputum. A marked secretion, an exfoliation of mortified tissue, the appearance and, subsequently, the rapid multiplication of the bacilli in the sputum will not occur until, as is frequently the case, the symbiosis of the tubercle bacillus with pyogenic organisms has taken place. Even here it is always questionable what causal connection exists between pyogenic organisms and bacilli, which species must prepare the soil for the other, and what constitutes the advantage of their working together. Many questions along this line are still awaiting solution, and we must not be induced, by the apparent ease

with which experiment removes all doubts concerning the spread of infection, to suppose the same distinctness also in the domain of human pathology. We should continuously bear in mind under what conditions the carriers of infection act in the experiment, being introduced directly into the blood in large quantities of pure cultures and with the exclusion of the ordinary protective measures of the organism.¹ Naturally, in disease caused by injection (the result of experiment), almost all defensive and compensating measures must not be taken into consideration, whereas these defensive elements are precisely what constitutes the enormous difference between experiment and normal infection in the human being. These elements, by their gradual appearance, produce a sum of functional changes which are accompanied with noticeable and unnoticeable disturbances of tissue, serving to develop the picture of the morbid process.

Let us examine a little more closely the main processes in both pathological conditions. In the one case (infection in the realm of human pathology) we are dealing with sharply defined phases of the processes of infection and incubation (development of the generator of the infection); we note a slow fixation in certain localities and a gradual development into a general affection, finally involving the entire organism. The other case (experiment) shows us how the *organism is suddenly inundated* with microbes and masses of ptomaines and toxins in culture, so that infection and acme of the disease are almost simultaneous, whereas the period of incubation is absent. In the former case there is the action

¹ Abnormal conditions prevail also in every case of experimental feeding and of inhalation tuberculosis.

of a noxa, probably very slight quantitatively, which is very likely to experience dilution while traversing its first route. The experiment, avoiding all defensive agencies, introduces into the blood large quantities of microbes in pure cultures—therefore, probably of a most virulent nature. Considering all these different conditions, is it to be wondered at that the final results in both cases are vastly divergent? What reason can there be to assume identity of processes when one, taking place in the clinic, shows in *every case the effect of individuality, of predisposition*, whereas the case called forth by experiment does *not at all* manifest these factors? If of one hundred human beings exposed to the same contagion only a *minimal percentage* falls a prey to illness, whereas in experimental injection *not one* is ever spared, how is it possible to speak of even a similarity of the phenomena? Indeed, under such conditions, it is not astonishing that the therapeutic results also are so very different that, according to the best observers, the *curative inoculation in disease caused by injection* is successful in all cases, while such results are not obtained in *infectious diseases*. In fact, the mere *possibility of curing all affected individuals by an identical process, if possible by an equal dose of the same remedy, is bound to arouse suspicion*, since we know from human pathology that the mortality of infectious diseases with a prolonged period of incubation (except measles) is always quite considerable, and that there is scarcely any question of an efficacy of specific methods of treatment in diseases that are so very different etiologically. Besides, there is a further fundamental difference between disease caused by injection and that produced by infection! The former concerns all individuals, including those with *normal* resisting powers,

because the injurious principle is introduced directly into the circulation, whereas in disease of conventional character, as above explained, only individuals are affected that are below par, whose vital energy is less than normal, being determined by the power of its resisting apparatus. Is it not natural that in the animal experiment—*i. e.*, in normal individuals—the protective inoculation is potent even after the outbreak of the disease, notwithstanding the magnitude of the infection, as, after all, neither a more marked immigration of microbes into the tissues nor a material injury of the infected organism can have taken place within the brief period of time which intervenes between febrile rise of temperature (effect of the injection) and the protective inoculation? It can be a question only of an interval of twenty-four hours, during which, probably, only the mechanical effects of smallest emboli become manifest. It is not difficult to imagine that the inoculation substance soon exerts its effects upon the cells which, to the greater part, being in a healthy condition, are still capable of reaction, and which readily respond to the influence of the vaccine virus. Only after the cell, in its prolonged struggle with the toxin, has experienced another distribution of internal labor (therefore, after its capacity for reaction has undergone a change) does the influence of vaccination become extinct—an influence, in fact, which represents a considerably smaller irritation than the one to which the organism is exposed by the primary, virulent, *injected* agent; for the product causing immunity—the vaccine—is in itself a somewhat mitigated product of homologous microbes, and will, therefore, call forth less cellular activity than the finished products of strong organisms, and that in proportion to the difference

between the mitigated products and the normal terminal stage.

It will be seen, accordingly, that these apparent contradictions as to disease by injection and disease by infection may be satisfactorily explained if we remember that the latter are two entirely different processes which must not be compared, much less considered equal, to each other.

However important *for the biology of micro-organisms* laboratory experiments are *under certain favorable conditions*, none of the conclusions arrived at from test-tube observations—and this view is constantly gaining ground—can be utilized in practise, since very simple conditions are present in the first instance, whereas the lasting fixation of conditions in the living human being is almost entirely beyond our influence. The essence of organic life consists, after all, in regulating, in spite of foreign influence, normal function in such a manner that the real conditions of life of the protoplasm of the most important parts are altered as little as possible. The medium, therefore, the nutritive soil, is changed continually; the quiescence of the invading germs is not an absolute one, as these may be washed away or eliminated. Nor must it be forgotten that every substance newly incorporated into the body, be it remedial agent or poison, at once calls forth changes (reactions) in that same body, and that its final effect is fully dependent upon these influences. The great difference between *dead* nutritive soil and a *living* organism is just emphasized by the fact that *no defense and no reciprocate action* take place in one case, whereas, in the other, these factors *exclusively govern the final result*. The dead soil is entirely at the mercy of the micro-organisms, provided certain conditions are

complied with; the living organism is not. The decision, accordingly, whether a remedy is antiparasitic—*i.e.*, whether it impairs or obviates the conditions favoring the life of the micro-organisms—can *easily be reached in the test-tube; with difficulty or not at all*, however, *in the animal organism*. In the former it is easily and exclusively brought in relation with the micro-organism that is to be tested, whereas a direct contact is entirely beyond our influence in the latter instance. But even if such a contact could be rendered feasible, it always remains questionable whether, upon these substances encountering micro-organisms and cells of the highly organized animal body, these latter might not be the ones that are more subject to influence. Protoplasm-destroying and albumin-coagulating substances that render the dead soil sterile to the promulgation of micro-organisms are generally harmful to the body. They are more apt to kill the cells of the organism, the defensive means of which they should reinforce, and, therefore, many of the laboratory bactericides, even in diluted form, constitute poisons to all higher organisms.

The prevailing effort of the present day to concede greater importance to results obtained by experiments than to clinical observation, and to solve questions of pathology not by the apparently more laborious method of utilizing copious clinical material, but by cutting the Gordian knot with *one precise* experiment, is fraught with danger that can not be too strongly stated. Enticing as it may be to ask direct, most simple questions of nature, and to obtain immediate and directest, apparently unobjectionable answers, we should always bear in mind that precisely this apparent—not actual—simplicity, this treacherous analogy of conditions, will tempt us to con-

fuse entirely different processes. We are led to underrate the complicity of morbid processes in the human and animal organisms, and to allow too great an influence upon medical thought and activity to one-sided and narrow theories resulting from this underrating. Because in medicine so-called scientific achievements (all new experimental results are indiscriminately termed scientific, with an absolute misconception of the value of induction) are at once passed as current coin in active practise, and thus are bound to obtain a conspicuous influence upon our methods, for this very reason it behooves us to call a halt to such a proceeding as will necessarily lead us to underrate the inexhaustible source of knowledge—observation at the bedside. To place experimental above clinical examination is sacrificing the end to the means. It may not always be easy to see our road clearly in the complicated mass of symptoms confronting us at the bedside, nor is the material to answer a certain question always unobjectionable. On the other hand, *the great variety in which the phenomena present themselves, the various conditions and view-points under which they are manifest, furnish to those that are able to see and to reason not a one-sided, but a thorough, survey of the vital processes in a mechanism which, altho most complicated, is transparently arranged. Only we must not demand, while still in the infancy of biological research, that we should succeed in solving all the riddles in that complicated instance of the struggle for existence which we call disease.* Experiments only furnish us with remote analogies, with apparent explanations. They serve to point out how far we still are from the final aim of a more thorough insight into these processes. They often represent, as it were, the desire of a child to ascertain

forthwith the laws that govern an ingenious apparatus by smashing it and exposing the wheels. Whenever experiments were falsely credited with being instrumental in strikingly demonstrating certain laws of function; whenever the belief prevailed that such an experimental result would be conducive to a better understanding, further observations have shown this surprisingly clear insight to be erroneous. We were apprised that we were on the wrong road, and that a laborious but many-sided clinical observation of the patient alone offers a guaranty for a safe, if slow, advance upon the path of research.

I am fully aware that my criticism will be called a retrogression, but I am convinced that it is well-founded. I do not demand that *exclusively one domain and one method of investigation should be cultivated*, but I merely give it as my opinion that *the clinic and the observation at the bedside should be considered the only scales* by which results obtained through other methods of investigation must be measured. *All laboratory methods, by whatever name they may be called, are only makeshifts, because they artificially imitate disease; they are able to touch upon only the extraneous aspect of matters.* They may show some objects from a different view-point, but they will never present the vital point: *the origin and development of the functional disturbance, the ingenious compensation as manifested by the struggling organism under peculiar conditions.* *They can never be identical with the real mechanism and with the nature of regulative processes encountered as symptoms at the bedside.* Experiment, correctly undertaken, enriches scientific knowledge; but it must not pretend to be the guide of practical action at the bedside, for it shows only the limits of compensatory capa-

bility, not the form of compensation. Experiment only in a few instances is thoroughly able to illustrate in the animal the clinical manifestations which we encounter in man. It may be done in certain infectious diseases in which the quasi-natural mode of infection is identical with artificial infection, or in such cases in which approximately equal conditions can be created for the experiment in that the (subcutaneously introduced) carrier of the infection is of such minimal quantity as is usually the case in infection of healthy human beings.

III

DISEASE FROM THE VIEW-POINT OF THE LAWS OF ORGANIC DEVELOPMENT AS A SPECIAL PHASE OF THE STRUGGLE FOR EXISTENCE

IN order to reach rational therapeutics, we must place ourselves upon a much higher and more comprehensive standpoint than the generally accepted one that disease is to be looked upon as something pathological, parasitic, as a curiosity, somewhat as in past times malformations were collected and classified as mistakes of nature before it was recognized that the same laws hold good for them that obtain in organic nature generally. *The same laws that govern the normal (phylogenetic) formation and development of the organism are equally potent in the domain of pathology.* Here, too, there are certain hindrances which create retardation in one place, increase in another. *Disease can only be looked upon as one of the many manifestations of the battle for life. It always follows the same laws of development to which the whole of organic nature is subject, for disease is only one of the factors active in the selection of individuals or nations, in man as well as animals.*

In the fight of organisms, as old as organic life itself, there have been developed by all beings certain defensive methods calculated to defend the individual and its kind against all external influences found in this fight for existence, and to make it possible for that individual to maintain its existence in spite of all obstacles. The organism reacts to distinct, increased irritation in a

definite manner. Whether this reaction is a suitable one in every instance can only be determined by a mind that recognizes the causes of processes, and not merely their external manifestations. The better understanding of these processes constitute a progress, the consequence of which is a direct causal, or at least aimful, symptomatic therapy. It would be an absolutely wrong conclusion to confound this latter with symptomatic therapy in general.

Looking upon disease as one instance of the struggle for existence, it is readily conceivable why, unfortunately, therapeutics is able to advance but slowly; for it aims at nothing but, by protection of the individual, to accomplish what nature, owing to its slowly developing processes of accommodation, has only in part succeeded in doing. Pursuing this line of thought, that therapeutics might be one of the means in the struggle for existence, would open up what a marvelous perspective! Therapeutics, which to-day justly seeks its chief aim in the prevention of disease, should become an essential factor in the battle for existence. It should be able so to alter the vital conditions of certain species of organisms that one (man) thrives and the other (pathogenic microbes) is exterminated; for to guard man against disease is equivalent to limiting microbes, which are located exclusively in the human organism, in their nutrition to such an extent that they are finally destroyed. What prophylaxis should accomplish in this respect would in the same manner be attained by the discovery of specific remedies which would be absolutely efficacious in all cases of disease due to the invasion of a certain microbe. Our interference in such instances would be the tool, as it were, employed by creative and destructive nature to preserve or to destroy its creations. The above

does not by any means pretend to represent a teleological conception, but it intends to express merely that our interference constitutes one of the mechanical processes which are neither means nor end, neither cause nor effect, but only preliminary conditions for another form of manifestation following it with mechanical necessity.

Dare we think it possible that our therapeutic actions could form such an effective remedy in the battle for existence? Does knowledge of the history of organic nature entitle us to hope for such discoveries, when up to the present the dying off of some species of organism is merely due to essential changes in their conditions of life in general, not to the activity of some other species? How will, in such a struggle, the faculties of accommodation hold out? These questions can not be solved here. They are merely brought up for discussion, since the standpoint taken in regard to them is not without influence upon therapeutic views and actions.

It is only as if we acknowledge the prevalence of the principles of the theory of development also in that special instance which we call disease that we will be able, in our opinion, to guard ourselves against Utopian hopes in the realm of therapy, just as he who understands the law of the conservation of energy will desist from hoping to construct a perpetuum mobile.

If disease, then, furnishes an important example of the battle of two species of organisms, or at least of the struggle of one genus against external influences; if different forms of organisms, simply because they exist, have equal claims to existence and proliferation, then it is obvious that *with the extermination of a bacterial disease there is possible the extinction of a species*. It is further evident that should one species be capable of finding

remedies not only for the defense of the majority of its members, but for the safety of all, this would cause the *conception of mechanical propagation and accommodation* to disappear from the domain of organic life ; for a species which is in possession of absolute protection, and which, according to the laws of nature, is to a great extent a condition of existence for other species of animated organisms, would entirely crowd out other genera, not according to the *mechanical law of causes* which dominates organic development or is manifest in the latter, but according to the *principle of limited practicability* (for its own species). It might be stated that such a result would prove precisely, and with mechanical logic, that the destruction of the other species had been the preliminary condition for the proliferation of the one that was in possession of protection. It might be said that man exterminated the bison not so much by killing the individual animals, but by cultivating the soil inhabited by the animal, in robbing it of favorable conditions of existence and preventing its propagation. It might also be quoted that the gradual drainage of swamps had already diminished the carriers of malaria, and that, in the course of time, these would be entirely exterminated. Utilizing all these facts, we might be tempted to believe it demonstrated that, after all, cases exist which show strikingly the capability of one species to destroy another through its own activity. However, we should always bear in mind that we are, in such instances, dealing with beings that find conditions favorable to their existence also outside of the body of man (or animal), whereas man himself—and probably exclusively—is the soil for many species of parasites in which they are able to live and to multiply. Let it not be forgotten that it is very difficult,

under complicated conditions of life, to protect this soil in all instances from the attacks of the germs—*i.e.*, to prevent the entrance of the latter into the body, or to arrest the spread in the organism already infected of those germs that have entered, and to inhibit the transmission upon individuals in the surroundings of those that were infected first (contagion). We might succeed in accomplishing this only after we had discovered the conditions of existence for the conduct of the smallest organisms outside of the carrier of infection, *and therefore had realized the full extent of their natural biological conditions (not only that fraction which we observe in the test-tube)*; then we might possibly be able to protect ourselves from the germs either by arresting their development, as in malaria, or by avoiding their ingestion, as in trichinosis—against which protection (possibly an absolute one) is feasible if we partake of its carrier, meat, only in a cooked condition.

However, two view-points should be remembered which are of importance in judging therapeutic possibilities—*viz.*, the *period of time* required to destroy the conditions of existence of one species, and the *processes of accommodation* which cause the struggle to be so varying, sometimes exposing the defending species to more violent attacks, sometimes opposing the assailants with better means of defense. *Accordingly, hygiene and prophylaxis will not be able, for some time to come, to exterminate existing diseases.* They will protect some individuals, but general protection will remain hopeless as long as we do not undertake it from all possible points of attack. It is sure to remain hopeless so long as we do not know the biology of the smallest organisms any better than we do now, altho we flatter ourselves to have discovered it

—in the test-tube. Is any one able to state with certainty the brooding places of the microbes of typhoid fever, of diphtheria, and of scarlatina, and by what medium they are transmitted? To carry on, with *remedial agents*, the *struggle of annihilation* against the organisms, it is immaterial whether the contest is waged in the domain of prophylaxis or in that of therapy—appears to be still *more hopeless*; for, whereas that part of hygiene which strives to destroy the hostile organisms in general is capable, after generations, of attaining its end (at least, within certain limited districts), the struggle with remedial agents, having for its object single individuals only, is merely able to save single individuals; it fails to consider the host of enemies existing outside of the human body. *We would never be able to exterminate malaria by administering quinine to every patient while permitting the stagnant pools to exist. The search for specific remedies, therefore, is not the prime end to be attained; it is but a limited one. It protects the individual but not the species, whereas hygienic precautions, if properly handled, not only deliver the external media in which we live of our enemies, but also improve our mode of living, and so go to the root of the evil and protect one species by destroying another.* Besides, so-called *specific remedies* are able to protect only a *small fraction* of individuals, who, once exposed to the pathogenic agent, have attained a state of diminished resistance owing to circumstances favoring the microbes and impairing their own condition. They have become weakened by the unaccustomed external conditions because they must apply a part, and often a very essential one, of the energy necessary to *their own preservation, to compensate* for the increased bodily activity resulting from unfavorable external influences. The

energy at their disposal to fight the invading noxæ is less, therefore, than under conditions that are adequate to them. *The specific remedy, accordingly, is able to accord protection from disease only for a brief period of time, and affection having once taken place, will be of permanent service only if the unfavorable external conditions are removed at the same time.* This truth is exemplified by the relatively small prophylactic and curative utility of quinine in malarial districts (small in proportion to the action of this drug in our latitudes), some observers even warning against the prophylactic employment of quinine, as the attacks are only postponed but not prevented, and they occur later on with renewed vigor. *A specific remedy against all individual cases of a certain disease does not exist in any instance.* A remedy can only be effective, generally, in mild cases, provided certain conditions prevail, and *this effect will be the less in regard to the duration of the cure the more rapidly the remedy is eliminated.* *For the specific remedial agent is distinguished from vaccine in that it actually requires a chemical alteration of the nutritive soil; consequently, it can be active only as long as it is present in the cells, whereas vaccine calls forth an intramolecular (physical) change, the duration of which may be quite considerable, as is emphasized by vaccination against smallpox.* Similar conditions prevail in the inorganic world, as when iron, brought in contact with a magnet, becomes magnetic, and remains so for some time after separation.

We have mentioned above that an impairment of the conditions of life of an organism (in this instance, the human body) facilitates the entrance and the colonization of carriers of infection surrounding it. It creates, as it were, the soil for their activity, in that too large a

portion of the total energy at the disposal must be applied to the compensation of demands created by the altered external conditions, thus considerably limiting the power of resistance to the entrance of a noxa, or to fight one that has already entered, and, above all, materially restricting the amount of energy necessary to perform the functions of the body. *The condition of the organism at the moment of the action of the pathogenic microbes*, therefore, plays an important part in the inception of disease, as is evidenced by experiments on rats immune to anthrax, which become susceptible to the disease by a vegetable diet—*i. e.*, inadequate food.

Applying the law of the battle of species against species to the special case of infectious diseases, it will run thus: the more favorable the external conditions are for the one, the more certain it is that, in certain relations of one species to the other, the weaker one becomes the nourishing soil of the stronger. From this we may conclude that one species will suffer defeat within a limited space of time, provided the single individuals representing it are continually under injurious influences—*i. e.*, such as are not in harmony with their natural conditions of life. It is the more bound to succumb the more the influences incongruous to it are simultaneously favorable to the other species battling with it for existence and, therefore, intent upon its destruction. It may further be inferred from the above that *disease* (by infection) may be caused by an *especial strengthening of the assailant* quite as much as by a *primary unfavorable action upon the invaded species* (*weakening*), and also that the possibility of an onset of disease is much greater if both conditions cooperate.

No experienced pathologist will dispute that, notwith-

standing the unquestioned presence of tubercle bacilli in all localities, in spite of their particular abundance in certain places (hospitals, prisons), the probability of becoming infected by these bacilli exists only for a very small percentage of those exposed to the infection; further, that a large number of the affected persons primarily presented to the experienced physician certain signs characteristic of distinct weakness of the organism. In view of the demonstration in thousands of instances that such a weakness of the individual is characteristic, even a physician who is ignorant of the law of the struggle for existence will not be in doubt regarding the serious part which this inferiority is bound to play in the combat against the tubercle bacillus, and he will at once predict the final victory of the latter. He will be still less in doubt regarding this part if the power of resistance of patients who are predisposed to the disease is diminished by external conditions, or if the dangerous nature of the pathogenic agent is directly enhanced by certain circumstances—for instance, by ill-ventilated rooms and by accumulation of microbes. Important, therefore, as the experienced physician must consider this predisposition of the affected individual—those that are not predisposed remain in good health even under quite unfavorable conditions—as little will he be inclined at present, unfortunately, to transfer to *the species* this importance of predisposition for the well-being of *the individual*, and to conclude that an infectious disease *taking place simultaneously or successfully in a great number of individuals* in the form of an epidemic depends upon such a *general predisposition*, and that *the soil for the occurrence of an epidemic is prepared only by a certain weakening of the powers of resistance of a majority or at least of a con-*

siderable number of persons living under the same external conditions.

Whenever enteric fever has developed very extensively and intensely during a war, no one ever doubted that this was due to the deterioration of the external conditions of life. However, in such cases the ease with which the virus may be transferred was remembered rather than the weakening of the powers of defense, the lessening of the resistibility; and even if this position was adhered to, no practical application was made of it in endeavoring to explain the origin of other epidemics. Yet such a conclusion is quite obvious. *Why do great epidemics, such as cholera, occur so rarely with us, altho, with the modern manner and continuity of travel, germs are surely transmitted to us? Why do some epidemics, such as measles, scarlatina, typhoid fever, sometimes present periods of acme and at other times periods during which they are entirely latent? Why is it that sometimes endemics, epidemics, and pandemics occur suddenly when even sporadic cases of these diseases were scarcely observed for years? Why does the devastating epidemic which affects the common fly, a disease characterized by the enormous development of *empusa muscæ*, never take place until the latter part of summer when, according to the natural course of events, the fly approaches the end of its existence? Why are preferably children affected by diphtheria, measles, and scarlatina? While the last question will receive the universal answer that the infantile organism manifests a special tendency to infection by the above generators of disease—the objection that then adults should not become affected by measles is not after all conclusive, since adults may have preserved certain properties which are usually peculiar only to the*

infantile organism—several answers will be in readiness to questions regarding the periodicity of cholera epidemics, and with reference to the periods of latency of diseases that are of more common occurrence with us.

Our hygienic and therapeutic measures which enable us to prevent the outbreak of disease, or to stifle the outbreak in its incipiency, will be brought forward—wrongly, in our opinion, since experience teaches that here, too, our achievements are limited. Unfortunately, an objective observation has taught, according to my conviction, that *what we so proudly look upon as our success is nearly always nothing but the expression of the natural course of events in the final result of which our activity is neither a noticeable nor important factor.* The means and methods which we have adopted against epidemics—naturally, those measures are the most effective which were employed last—*appear to be helpful simply because the epidemic happens to become spontaneously extinct.* But we explain this coincidence in the sense of a causal relation, and, owing to a temporary triumph at the power of our achievements, deprive ourselves of the faculty of seeing more clearly in such important questions. Any one who does not share this opinion may attempt to answer the questions above propounded. Why, then, is it that sometimes we are powerless against disease, whereas at other times we apparently master it, having in *both instances* usually employed the *same* remedy and the *same* method? Why do cases of diphtheria get well under the same régime in one period, when at other times most of the patients succumb? The answer must be that *the apparently identical conditions of both epidemics are not really identical after all,* since we are by no means familiar with the external conditions which,

so far as the realm of medicine is concerned, influence the combat between two genera of organisms. We are only able to infer the presence of such conditions as will decide the outcome of the struggle from analogous observations in other domains in which the battle for existence is likewise raging. Organisms arise and disappear, they develop in large numbers and they diminish, *because unknown factors favorably or unfavorably influence the conditions of the species that are dependent upon one another, and because generally the element which is favorable to one is at the same time detrimental to the other.* Why were the forests of Germany devastated during the last years by the ravages of the army-worm?¹ Why did the individuals of this species multiply so enormously after nothing had been heard of them for so long a period? The answer must be because certain preliminary conditions were present for a favorable development which did not cooperate during former years. Why does phylloxera spare some wine-producing countries and invade others? Because it does not everywhere find the conditions favoring its existence, and because some species of vines, possibly on account of their great age, are not as resistant as others. Why does the enemy of flies, the *empusa muscæ*, develop only toward the end of summer? Because the nutritive soil of this organism, the flies, is weakened in resistance at this time. The above does not mean to be an explanation of these processes, but merely to point out that we must not form one-sided opinions of conditions, because many possibilities have not been considered in just those cases in which we believe we recognize the causes quite clearly.

¹ A kind of caterpillar (*phalæna bombyx monacha*) which migrates in large flocks.

Applied to the present theme of the infectious diseases, we enter the objection that it is wrong to ascribe the origin of all these affections exclusively to the action of microbes. It must be demonstrated that the mere presence of minute organisms in diseases is not sufficient to explain the nature and the mechanism of the affection. It must be emphasized that much study must be applied to the investigation of circumstances, which, in the presence of the so-called generator of the disease, only furnish the essential preliminary conditions for its successful action. So far it has been quite falsely presumed that the conditions favoring the thriving of microorganisms should be looked for solely in their external (exoteric) circumstances. It was assumed, for instance, that the cholera bacillus might be transmitted, but would not be capable of infecting because it could not find the preliminary conditions necessary to its development in the soil. It was assumed that the height of the ground-water [*Grundwasser*] is in a similar relation to the development of the typhoid bacillus, and that certain conditions of the ground-water favor an increase of the typhoid germs, and with it the outbreak of an epidemic. These facts are surely correct, and it is quite conceivable, from the standpoint of the struggle of the organisms, that conditions which have become more favorable for the existence of a species enhance its faculty of becoming harmful. This, however, does not yet account for the second factor: the weakening of the attacked organism—very wrongly, in our opinion, since generally not the intensity of the pathogenic organism plays the principal part in the infection of the individual, but the *predisposition*—*i.e.*, the weakened condition—of the attacked, or a coincidence of

both factors. Those cases are very rare in which the cause of the affection is due to the large numbers and to the virulence of the microbes. The predisposition of those that are actually infected plays a part even in ill-ventilated sick-rooms, in localities in which greatest numbers of bacteria are deposited, in so far as these unfavorable external conditions must exert their detrimental effect also upon the human organism. Neither employees of prisons nor hospital nurses become more frequently affected by tuberculosis than other individuals that are not predisposed, living under favorable external conditions—for instance, in the open air—whereas *prisoners* are notoriously very often affected. And if, as is claimed, the members of certain religious orders of nurses are said to fall a ready prey to tuberculosis, this does not, in our opinion, constitute a conclusive proof that the affection is caused by the special chance of being infected—owing to more favorable conditions for infection—but is due rather to the weakening effects of the occupation and of the peculiar conditions of convent life upon the individuals in question. Allowing, therefore, that cases of infection actually occur in which a special activity of the generator of the infection must be held accountable—which, however, are not very frequent—it must be emphasized that the *ever-changing predisposition of the single individual and of communities of whole nations—yes, of the inhabitants of an entire hemisphere—plays the principal part in epidemic diseases.* An epidemic breaks out, not because at other times no germs were transmitted or had developed, *but because at stated periods communities or nations, owing to influences unknown to us, are in a condition that is particularly adapted to cause an infection by a certain microbe.* This was strikingly shown

by the last epidemic of influenza which, in our opinion, should not be ascribed to a new microbe, but to the peculiar climatic conditions that at that time prevailed upon our planet. These peculiar climatic conditions called forth a weakening of the organism and a predisposition to disease, which was promptly utilized by our constant enemies, the pyogenic organisms and streptococci. Why might it not be possible, even if we do not know the full extent of the preliminary conditions required to weaken the human organism, which are most certainly expressed in some climatic factors, that such unusual atmospheric phenomena as were evidenced during the last years in shining clouds, in phenomena appearing at dusk and dawn, and ascribed to an extraordinary diffusion of dust, might not also be capable of influencing what was formerly called the *genius epidemicus*—i. e., our conditions of existence? What opposes the conception of them as the signs of a change of the extraneous conditions under which we live, and thus as the precursors or accompanying manifestations of certain effects upon the human organism which are inseparably associated with them? We need not, altho it seems quite obvious, even here construe a causal relation between the phenomena, but may consider them as the expression of certain processes caused by mechanical factors, which, in spite of their simultaneous occurrence, must not necessarily be in the relation of cause and effect, altho it may be possible that such is the case.

I do not know whether these discussions will find endorsement. To be candid, I do not expect it, since the experimental proof is lacking, and since the present generation, firmly in the clutches of prevailing bacteriology, and denying all facts determined by experience regard-

ing the influence of predisposition, admits only of micro-organisms as the causes of every infectious disease. Activity of bacteria is certainly and inseparably combined with the origin of certain diseases, but it is only a cause of disease when the indispensable preliminary condition—a weak or weakened organism—is present.¹ It would be more nearly correct, therefore, and would avoid misunderstanding, not to use the term “cause” for the rôle played by the microbes in the origin of disease, and to say instead: The cause of the disease is the weak body, whereas the impulse to affection—*i. e.*, the production of an altered condition of internal functions—is given by the presence of certain micro-organisms. For we also say: The cause of the falling of an object is gravity, not the accidental cause (the process of producing the effect) which gives rise to the fall of the object. However, whatever opinion we may form regarding the part played by the organisms that represent the combatants, this much is certain: that disease is only a special instance of the struggle for existence, and that in each individual instance (case of disease) and in each phase (epidemic) the laws of adaptation and selection, which dominate organic nature, come to the front. The final result of our participation in this struggle, therefore, the part which we call therapy, is also subject to these general laws, and it would be utterly wrong to believe that we are in a position to force any decision which is at

¹ Experiment and the predominating study of test-tube cultures have served to obscure the true state of affairs, since they tend, most unjustifiably, to minimize the individual predisposition of the infected person, and to overestimate the ability of the microbes to infect in every instance. It is true, in producing experimental infectious disease in which the micro-organisms from cultures are introduced in great numbers and directly into the circulation, the effect of the microbes alone is in evidence, but it is manifest against an almost defenseless enemy.



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variance with the laws of development in nature. In those cases in which such a result is hoped for, the wish is the father of the thought, and in those instances in which it is believed that such a result has already been accomplished, disappointment has stood at our elbow, as the history of medicine shows at every point.

IV

CONTRIBUTION TO THE HISTORY OF THE MEDICAL CLINIC, AND OF THE THEORIES GOVERNING THE SAME

THE development of the theory of pleurisy furnishes a true picture of the history of the medical clinic and of the theories governing the same. The influence of theorizing and empiric, of localizing and generalizing schools, is nowhere more in evidence than here.

Whereas some considered only the picture of disease as a whole, and looked upon local manifestations as the accidental expression of a change in the constitution and of the fluids of the body, others regarded the essence of the affection to be represented by the local process; accordingly, they endeavored to determine the local signs of the affection and to utilize them in judging of processes of the tissues. Whereas the former could look upon changes of the tissues of the pleura as being identical with and equivalent to changes in the pulmonary tissue, and, accordingly, often overrated the symptoms of the general disease in comparison to the local affection, the latter went to the other extreme, and, considering all the signs of the altered reaction, they created almost countless forms of the affection, *quasi* a new species of an artificial system.

These endeavors reached their climax when the doctrines of *pathological anatomy* ruled clinical medicine. The utmost limits of possibilities were reached in the attempts to adapt the rather uniform results of clinical

investigation to the manifold pictures furnished by pathological findings. Great pains were taken to analyze the few main categories of clinical signs into a multitude of irrelevant details, as if to the symptoms of visible changes, of the reaction of the tissues, and of the visible alteration of the function, there always corresponded the adequate change of the internal, invisible work of the tissues, the same amount of energy developed, and the equal formation of strength—*i. e.*, the same amount of expenditures.

When the *new methods of diagnosis*, auscultation and percussion, furnished to those who, until then, were familiar only with the general symptoms, remarkable disclosures regarding local changes, a belief gained ground that prognosis and therapy might be derived directly from the *physical changes*. Entirely misjudging the fact that a physical explanation of the symptoms should be preceded by a thorough knowledge of the dynamic and biological processes, of the relation between *visible work* (reaction) and *invisible work* for the development of energy, the erroneous belief naturally became prevalent that the visible alteration of the *volumen* or of the consistence and motility of the tissues and organs, a condition which we designate as disturbance of tissue, anomaly of function or symptom, was identical with the *internal processes* of the formation of energy, whereas simple consideration teaches that the visible function corresponds to an equal alteration of the account only when the capacity for reaction, the original stimulability, the proportion of the process of causation, is equal to the amount of work performed. But any one who means to conclude from the amount or from the form of the reaction upon the consumption and store of energy in the

organism, commits about the same mistake as he who would determine the kind and size of the substratum producing sound waves, or even the number of possible detonations, from the intensity and quality of the explosion.

After a period of rushing enthusiasm, abundance of observations and the criticism of unbiased investigators have shed light, as was to be expected, upon the true value of our methods, and upon the difficulties of judging of functions based solely upon certain acoustic phenomena. The conviction has gained ground that *no method furnishes pathognomic signs—i.e., signs which permit of simple inference, and that a sign in itself means little, since only the combination of all signs shapes the picture under the influence of the synthetic and analytic capacities of the observer*, just as the comprehension of an object or of a process becomes the more perfect the more we know of its essential qualities and are able to mold them into an entity.

In spite of all such phenomena, in spite of the fluctuations between overvaluing and underrating a method, which to those that know the history of medicine are nothing but the landmarks of new periods, new methods are constantly hailed with the same enthusiasm, since the hope of discovering the pathognomonic symptom is never abandoned. The dream is always repeated to solve the riddle of the formation and transformation of energy and of the first processes of causation in the hitherto usual manner, and to infer, from the results of external manifestations, the alterations of internal function of the visible reaction, whereas, after all, only a small portion of the transformations and only the grossest evolutions become manifest in the manifold forms of

reactions. To summarize: *Visible work and energy capable of being measured by this criterion are merely the final items of the expense account of vital force, the individual items of which are hidden, as is the size of the reserve fund and the various items of the receipts of vital energy (by waves of light, heat, sound, and of other natural phenomena coming in contact with our organs of special senses.)*

It was believed, even at a very recent period, that *bacteriological research* bade fair to solve the enigma of the origin of functional disturbances—*i.e.*, to isolate the long-sought-for *etiological unit*, the process of causation or stimulation. The conviction that it would be possible to determine definitely the cause of disease promised to fulfil all requirements of the physician. *The demonstration of definite forms of micro-organisms apparently furnished in the simplest manner possible the main points of support for diagnosis, prognosis, and therapy.*

However, unbiased clinical observation soon subdued the overzealous, and it was again seen that the pathognomic symptom existed only in the imagination of those that are unable, or unwilling, to know that the *sum total of the different reactions which we call disease or disease process presents only externally and in very superficial outlines the alterations of internal function* (of the formation of the energy instrumental in bringing about the cohesion of the organism). But we are as little able, from the manner and extent of this external performance, from the visible symptoms, to infer the amount of energy on hand which furnishes the opportunity for transformation of power and, with it, for the preservation of the engine, as to infer from the mere determination of the radiating heat of a body the *specific heat* or capacity of heat of

the same. If the latter is not known, neither the amount of heat present nor the work performed, or to be performed, can be recognized. If the quality of the *predisposition*, the amount of the stimulability of the organism, is unknown, the significance of the individual performance, of the symptom, can not be estimated.

Visible reaction being, therefore, a result of the invisible processes of causation and of the invisible faculty of developing energy, the *symptom*, therefore, to use medical terms, being merely a *function of stimulation and predisposition*, the solution of this equation with two unknown quantities necessarily presents an endless variety of results. The same stimulation with varying predisposition is bound to furnish as many different forms of reaction as does the same predisposition with varying stimulations.

Since what we perceive as reaction requires only a part of the energy on hand, and represents only the visible portion of the processes, we are unable to infer either from the amount of radiating heat the extent and form of the process that produces the heat, or from the work performed the transformation and the limits of the performance of the processes supplying the energy of motion. Accordingly, the result of *one* method of investigation, the form of reaction, the individual symptom, can furnish to the physician a basis for judging the case only when he is familiar with *the extent of the local and general predisposition or with the intensity of the stimulation*.

One and the same form of microbes—yes, the same quantity—is bound to produce, according to predisposition, different symptoms and clinical pictures. Different forms and quantities, again, may be accompanied with the same phenomena and with the same course if a

corresponding difference of the capability of reaction is present. It was possible, during the era of tuberculin injection, to study most minutely the differences of the reaction due solely to the influence of the individual predisposition, since the irritant (tuberculin) could be administered in any desired dose, and the extent of the reaction, especially the febrile, could be exactly determined.

In the interest of prognosis and therapy not only is the determination of the species of micro-organism present to a certain degree essential, but information as well regarding the *extent of irritability* to foreign bodies and their product (predisposition). The degree of the latter, however, can be inferred only from *clinical* viewpoints. The demonstration of the microbes is of particular value only in this connection: the presence of tubercle bacilli in the sputum proves a certain inferiority of the pulmonary tissue, which condition prognosticates further changes of tissue and also creates the soil for the pyogenic organisms.

The various species of microbes should be employed as *principles of classification of forms of disease* with the same restriction only as other elements of irritation are used for this purpose, since, at best, only an artificial system can be established in such a manner. A *natural* system can be derived only from a consideration of the various amounts and forms of energy that are to be taken into account in this instance and upon the basis of *functional diagnosis*. But, biased by unnatural classifications and not in possession of suitable methods for measuring the amount of internal work, we are still far removed from this form of judging disease. We are satisfied to *look upon the forms of disease as permanent manifestations, as conditions*, and therefore demand their class-

ification by a catchword, as if a satisfactory recognition would be attained by this diagnosis *à tout prix* (by labeling the disease), while in reality the only possibility offered us is to force the *manifold, continually changing processes in the body into the narrow horizon of a systematician or into the pages of a text-book.*

It would lead us too far to accord to the development of these view-points the space they deserve at this, the beginning of a new epoch in medicine. Our object here is only to illustrate the difficulties of judging the processes in a healthy and sick organism to those who consider *health and disease merely as special instances of the energy in the organism and not as objects of scholastic definitions* which, meagerly outlined from extra-corporeal points of view, of necessity have lost their value, since they do not represent the processes of life, but are mere abstractions answering the requirements of the human mind for generalization.

Medical activity will always remain the *art* of drawing from an abundance of facts, collected from different aspects and view-points, careful conclusions regarding the balance of energies in the body. It must not despise the experience of centuries, and it is bound to return to conceptions that, in the course of time, have proved themselves to be well founded—*i.e.*, approaching truth.

One of the most firmly established positions based upon experience is that of the *importance of predisposition and of the fallibility of pathognomic symptoms.*

Any one who attempts to apply a symptom and the result of a method for a direct conclusion upon that complexity of processes which we call disease will always be wrong, as will he who would derive a certain degree of temperature in an object from the combustion

of a certain quantity of coal, in disregard of the fact that the forms and the intensity of heat development vary considerably.

Let it be hoped that the time may not be far distant when it will be once more recognized that those who consider merely the local condition or a pathognomonic symptom proceed quite as erroneously as those who figure only upon the general pathological condition, and attribute absolute value as a criterion for prognosis and as basis for their therapy to one particular (general) symptom—for instance, fever.

With a purulent or ichoric exudate, even the strongest patient is bound to succumb or suffer a severe lesion if a local diagnosis by exploratory puncture or an operation should be postponed because the general symptoms apparently do not as yet require immediate interference, the condition of strength being fairly good and the temperature approximately normal.

Nor is it possible to form an opinion as to the true condition of a patient if only the local findings are to be considered, for a small exudate may be most serious, and a large one relatively harmless. Many a suppurative or ichorous exudate will, under the treatment of an experienced physician, heal more rapidly than a serous one which may form the foundation for a chronic process of the lungs.

True medical art will, when searching for local changes, remember the general condition, and, *by reason of its experience with reference to predisposition*, will correctly refer the visible local phenomena to the general reaction. A temperature of 104 degrees Fahr. in a child is frequently not as important as a slight chill in an adult, and it is well known that clouded mentality in

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children is often the equivalent of an uncommonly sound sleep of a grown person.

It is a sign of true medical insight to consider *symptoms not as the essence of disease*, but simply as an inaccurate picture and criterion of changes of internal functions, and, by careful observation of the effects of various irritations, to determine the extent of predisposition, which alone permits an opinion as to the sthenic and asthenic forms of reaction.

V

ON THE DOCTRINE OF THE EFFICACY OF SPECIFICS

AS YET there are, unfortunately, only two diseases for which we possess specific remedies, and usually acute articular rheumatism is named in the first place. For nobody will deny, in spite of occasional therapeutic failures, that salicylate preparations bear certain specific relations to the agent calling forth the clinical symptoms of the disease, the cases in which a prompt effect was accomplished forming the greater majority. It is true, if this effect is to be very conspicuous, according to our experience, the case must be a recent one, or several joints must be uniformly and not too markedly affected. The more violent the inflammation—not the swelling, which is by no means in proportion to the inflammation—and the more the affection is preferably localized upon *one* joint, the less will be the effect of the remedy. By *effect* we mean, naturally, the *prompt removal of all symptoms* and the reestablishment of free motion, not mere alleviation of pain and defervescence. It is possible, within certain limits, to establish a theory regarding the effect of salicylic acid, without adding too much that is hypothetical, when the following facts are remembered. Acute articular rheumatism may be conceived as a form of disease which is in close relation to the generators of pyemia, for, apart from the fact that the investigators of the disease have demonstrated the presence of such pyogenic organisms as are also found in the various forms

of pyemia, the clinical course and the manifestations of both affections must suggest this relationship to the experienced physician. The point of invasion of the toxin is usually not known in either case, and the joints and the serous membranes are the points of selection in both instances ; further, cases occur in which apparently well-characterized acute rheumatism passes into true pyemia ; finally, suppuration of individual joints is not a rare event in acute articular rheumatism. Such cases are the more convincing, since they demonstrate that in one and the same individual *some* joints present the *typical criteria of the rheumatic affection* (swelling and serous exudate as well as the prompt reaction to salicylate preparations), whereas other joints remain unaffected by the remedy and finally pass into suppuration. To assume a mixed infection in such instances would be to complicate a simple matter. The assumption is much more plausible that the affected joint, which often at the onset even appears as being more markedly involved, became, at the very *beginning of the disease, subject to a more violent invasion*, or formed a point of least resistance. The following pathogenesis of acute articular rheumatism may be looked upon as probably corresponding best to the clinical manifestations, since all observations can be most conveniently subsumed in the same, according to our opinion : The generators of inflammation and suppuration entering the body, upon circulating in the latter, are taken up by the serous membranes, which represent, as it were, the catching apparatus for certain forms of bacteria in which they may eventually be rendered harmless even without any local manifestations. According to their numbers and infective power, they here excite that *form of inflammation which is character-*

istic of serous membranes—at first, owing to their distribution over the entire body or on account of the peculiar condition of the cells of the serosa, the milder form. The more intensely a joint is affected, the more violent becomes the disturbance of the tissues, the greater the swelling of the parts, and the sooner *suppuration* takes place. If the virus has at the onset invaded the body in large quantities, a more or less well-developed, truly pyemic condition arises, causing suppurations in many organs. At the same time, the possibility must not be overlooked that also *different* forms of acute articular rheumatism, as well as other pyemic conditions, may be due to *different* species of pyogenic organisms. The process will, in general, take place in such a manner that the more bacteria obstruct the lymph spaces, the more will become manifest, besides the *active* increase of lymph secretion by greater activity of the lymph-secreting apparatus, and of the tissue itself, which, by the activity of its cells, furnishes the greater quantity of lymph, passive stagnation of lymph, in consequence of thrombosis of the vessels, and with it will appear the more marked local effect of the pyogenic ptomains or of the microbes proper. However, in order not to be misunderstood, we wish to emphasize that, even with passive stasis of lymph, we do not assume a filtration process, but that we designate by this expression only the impediment to the deflux from the peripheral to the central lymph channels. The secretion of lymph—whether taking place with mechanical obstruction to the deflux which raises the pressure, as does an increased supply, or with increased arterial pressure—is always an active vital process based upon increased activity of the endothelia of the blood-vessels and lymph-vessels, and of other

cells of the body participating in the secretion, not upon increased exosmosis of the membranes.

Guided by these premises, how shall we look upon the action of the drugs, especially of the surely efficacious salicylate preparations? It is evident, above all, that the remedy must actually be deposited in the joints, and that a drug can not be effective which does not reach the affected part at all or only under certain circumstances. We were forced to assume *a priori* that the salicylates answer these conditions better than other medicaments. This theoretical postulate is confirmed by the experiment which shows conclusively that iodine preparations so frequently employed do not reach the affected areas at all, whereas the salicylates can be very distinctly demonstrated in the serous membranes and in the fluid of the diseased and healthy articulations. However, our investigations also show clearly why the specific action of the remedy is manifest only in serous exudates, whereas a beneficent effect could be but rarely shown and only to a moderate degree in suppurative cases. This is due to the fact that the drug has no opportunity to display its effects, owing to the obstruction of the routes as well as to the intensity of the action of the pathogenic agents and, above all, to the affection of the tissue cells. The quantities of the drug actually reaching the joint are too insignificant to exert a noticeable effect. To this is added that the obstruction of the channels is an injurious influence, in so far as pus that is not absorbed continually acts as a new irritant upon the tissue cells and, therefore, that cure can not be accomplished until the pus has been evacuated by opening the cavity. Irritation will then cease, and the tissue cells, after destruction of the microbes that had colonized in them,

will gradually return to normal conditions, whereas the reestablishment of former functions naturally depends upon the damage done in the tissues of the serous membranes.

What ideas can we form of the effect of salicylates and of the other specifics in diseases due to the action of micro-organisms? The possibility of an explanation is given for quinine by the fact that *the plasmodia of malaria, as can be distinctly noted under the microscope, by no means abandon their motility even upon the addition of a very concentrated solution of quinine.* This observation shows that the *micro-organisms* are not *directly* deleteriously affected by specific remedies, even if employed in stronger solutions than usually. It follows that the effect can depend only upon an alteration of the nutritive soil necessary to the development of the plasmodia. The specifics merely deprive, as we must assume, the microbes of the faculty of propagation. Applying this deduction to the question of the efficacy of salicylate preparations, we arrive at the conclusion that of the three possibilities capable of explaining the influence of the above remedies—viz., anesthesia of certain nerve tracts, action upon the temperature, and the direct influence upon bacteria arresting their development—only the last-named can come into question, since this alone is capable of accounting for all existing conditions in a satisfactory manner. That it is merely a question of arresting the development and by no means of extermination of the intruder is probably shown best by the recurrences which, particularly in acute articular rheumatism, are so frequent, often appearing only after long intervals. Admitting that specifics possess the above-mentioned effect of arresting development, the processes, after the remedy

has reached the affected areas, would take place as follows: so soon as the microbes cease to multiply, the obstruction of the lymph capillaries and of the tissue interspaces by the micro-organisms themselves, or by the leucocytes migrating to combat the latter, is diminished or ceases entirely, lymph stasis decreases, and the activity of the tissue cells or of the white blood corpuscles suffices to destroy and to eliminate the pathogenic organisms and their products. The substances eventually produced by the small quantity of persisting microbes are rapidly rendered harmless and eliminated. The mere arrest of the propagation of the microbes is sufficient, therefore, to usher in the cure.

Accordingly, there is absolutely lacking any proof that micro-organisms are destroyed by specifics in concentrations as usually employed in the body—not to speak of the fact that it is *a priori* unlikely that, in a battle between two kinds of organisms, the highly organized body cell should withstand the action of any variety of protoplasm-destroying toxin—albumin-coagulating antiseptics must be considered as such—better than a monocellular micro-organism. Remedies that in a certain concentration are sure to exterminate some varieties of microbes would of necessity, even in comparatively small quantities, destroy the component parts of animal tissue. The effect of specifics, therefore, can not be a purely antiseptic, disinfecting one, but must be based upon the fact that the small, unquestionably efficacious quantities of a specific substance as usually employed in therapy alter the nutritive soil in such a manner that the invading micro-organisms are prevented from displaying the strength so fatal to their host. What we call predisposition to infection is nothing but the capacity for

furnishing a suitable soil; absence of this tendency points to an unfavorable condition of the nutritive soil. This "something" is supplied to the cell by certain remedies in proper concentration not affecting the vital activity of the cell about in the same manner (apologizing for the coarsely mechanical comparison) as wood is protected from the invasion of fungi—by impregnation with tar or by drying. The addition of a bactericidal substance to the nutritive soil necessarily acts upon the vital activity of the microbes, for they are no longer able with the same nutrition to accomplish as much as usual; for the sake of self-preservation they are compelled to consume more energy. It is one of the most characteristic properties of micro-organisms that they are capable of *propagation* only upon a favorable soil in which the processes of sporulation peculiar to them can be performed without impediment or restriction. At the very moment when they do not find sufficient nutritive material or a different strength exceeding a certain concentration of the soluble nutritive material, or when their own products have attained a certain maximum, the capacity for further development ceases—*i.e.*, for *multiplication*—and thus *they have lost, as long as this alteration of the soil persists, their most dangerous quality. The faculties of forming toxins* (selecting this expression as the most general designation for the products of metabolism of the bacteria and for substances foreign to the economy of the body which are formed by bacteria in the struggle with the cells) *and of propagation of monocellular organisms* are inseparably associated; *microbes that do not multiply are harmless*, since they do not develop toxins, and the *formation of such toxins again is a sign of proliferation and multiplication of the invaders.* To pre-

vent microbes from *propagation* by changing or impairing their conditions of nutrition means to weaken their virulence or to render it entirely harmless. How this is accomplished, whether by introduction of the products of metabolism of the bacteria, or by certain other substances (wrongly called antiseptic), either altering the nutritive soil or in some other manner interfering with the metabolism of the microbes, is immaterial. The fact remains that a remedy, *to act as a specific against micro-organisms already colonized in the body, needs neither be a bactericide nor reach even approximately the strength required to destroy the invaders. The purposes of therapy are well served if the remedy deprives the microbes of their dangerous capacity of propagation*, and thus of the possibility to usher in and keep up unlimited disintegrations in the affected body. Yeast may also be deprived of its splitting off properties without being destroyed at once if certain changes of the nutritive material take place which disturb its multiplication. Fighting for their own existence, endangered by an alteration of the nutritive soil—therefore, of the condition most important to their development—the microbes lose a faculty that depends solely upon unlimited nutritive material—*i.e.*, that of propagation. They remain alive, and after a certain period may again develop most actively, either having preserved their original form or having assumed lasting forms—*i.e.*, such as can exist even under the most unfavorable external conditions, being reinoculated upon a fresh nutritive soil. This is especially true when the microbes, as the artificial forms, *do not possess an active protective power*. However, they are temporarily harmless for the animal and human body, and may, in the course of time, be entirely eliminated by the active

forces of the body upon the regeneration of the tissues. Should the remedy be too weak, or the number of the micro-organisms too great in comparison to the regenerative faculties of the body, a recurrence takes place, a process which proves conclusively that the invaders were not killed, but had remained in a condition of sterility, of arrested development, and that, immediately after the effect of the remedy had ceased to be operative, the new formation and unlimited multiplication commences again.

VI

DISINFECTION IN THE TEST-TUBE AND IN THE LIVING BODY

THE treatment of erysipelas proposed by me (inunction of the adjacent healthy parts to a considerable extent with carbo-vaselin) has instigated Liebreich to a remark which, both because it questions the favorable results obtained, and because of the principal importance of the objection, offers a welcome occasion to reopen the subject. The dictum which Liebreich upholds on the basis of Gottstein's investigations—"Carbo-vaselin acts like carbolic oil, and an effect of carbolic acid can not be achieved in this instance"—can not be correct in this general form, since we already stated in our communication that the urine of the patient in some cases showed all the qualities of carbolic acid urine. Therefore, carbolic acid unquestionably did show its effect in this instance, and further investigations made by us for some time past (the results of which will be published at an early date), have demonstrated that large quantities of the antiseptic are absorbed even in the application of salicylate preparations in the form of ointments, the evidence of which is readily shown in the urine. The dictum of the inefficacy of the ointments, therefore, must not be as formulated by Liebreich. It could only run thus: a disinfectant or sterilizing action of antiseptics used in a fatty vehicle is excluded. However, this part of the question is entirely out of consideration in our

therapeutic proposition. We are not dealing with absolute sterilization concerning the micro-organisms that may enter from *without*, but with a protective measure for parts that are not yet affected. These, it is true, are deprived of an essential protective contrivance if the enemy has already pierced the bulwark of the epidermis, but the organism still possesses another means of defense in the energy of its tissue activity, which may call a halt to the further advance of the micro-organisms, as is proven by spontaneous recoveries in erysipelas. This means of defense, consisting in an occlusion of the channels through which the bacteria may spread, in absorption and destruction by ameboid and fixed cells, or in an alteration of the nutritive soil unfavorable to the development of the germs, may in part be strengthened by therapeutic measures; especially is it possible to influence the condition of the nutritive soil very materially by an incorporation of antiseptic agents. *Therefore, the results of culture experiments upon artificial soils must not be generalized and utilized for inferences upon the conditions of the living organism, since the living tissue is capable of leading to the fight independent means of defense, trained and tried in the struggle for existence, in that it either inaugurates and carries out chemical processes which deprive the invaders of their means of existence, or brings about a sterilization of the nutritive soil by the aid of certain antibacterial remedies, the concentration of which naturally must not act in itself as a noxa.* The organism is even capable of forming energetic protective agencies from substances which, mixed with an artificial soil or added to a developed culture, remain ineffective (owing to insufficient strength or because they are employed in the form of a salt). We know now that the

very effective iodoform, by its antiseptic influence, prevents development in spite of the fact that it contains micro-organisms, which, taken from it, may undergo further development on an artificial soil. We even know that, after the injection of anthrax vaccine, injection of anthrax bacteria remains futile, altho the micro-organisms continue to vegetate in the body of the immune animal and retain their virulence for a long period of time, as is shown by inoculations (Bitter). Thus we arrive, from a theoretical standpoint also, at the conclusion (which we have already proved by the demonstration of carbol and salicylate derivatives in the urine after employment of these medicaments in the form of ointments, and by the very favorable results of this method of treatment) that antiseptics, applied in fatty vehicles, exert their full effect in the organism. In our opinion, in order to obtain an ample effect of an antiseptic, it is necessary only to select the concentration so *that the absorbing tissues acquire an increased immunity without being also injured by the protective agent which in no case is indifferent.* Therefore, for certain purposes weak concentrations of the remedy are indicated which are not capable of injuring the energy of the tissues, altho they act upon the nutritive soil. For this reason we prefer a form of the ointment which acts more mildly to watery solutions which, without adhering firmly to it, cause the skin to swell, and do not as completely impregnate it with the antiseptic as do fats.

VII

STIMULATION, REACTION, AND PREDISPOSITION

THE terms "stimulation," "reaction," and "predisposition" have been so frequently employed in the discussion of the importance of the symptom that it seems necessary to direct our attention more closely to these conceptions which play so important a rôle in the explanation of the nature of pathological processes that they have even given occasion to the establishment of systems of their own. We must endeavor to trace them back to well-known physical processes, to represent them as forms of motion following certain mechanical laws. It must be shown how these vital conceptions, from the view-point of the law of the conservation of energy, may be traced back to molecular physical processes. We call stimulation *the cause of the production of that form of motion of matter which is designated as life*; we call stimulation, furthermore, any change of the external and internal conditions under which the protoplasm *lives*. We call reaction in its widest sense all forms of performance of work, displacements of atoms and molecules (or processes of a physico-chemical nature) with which the protoplasm responds to every change in the processes of causation—*i. e.*, of the external and internal conditions of life affecting the organism. This reaction exists even when the stimulation is ever so small; only it is not always demonstrable by the means at our disposal, since

it is a question of infinitesimal alterations of the molecular mechanism. Even the minimal quantity of living energy or heat which affects a body is bound to produce a minimum of motion in its molecules. An organic body is non-excitabile in which no stimulation, no living energy—*i.e.*, no continuously acting process of causation—produces transpositions in the amount of energy on hand ; it is dead when such transpositions can no longer be brought about by mere processes of causation. The problem of life is the stimulation of these processes of causation in every germ of a new individual, and its preservation during a stated period which we call *individual* life. It is obvious that, in the course of organic life, certain relations have developed between these stimulations originating in the connections of the protoplasm with the surrounding medium and the processes in the protoplasm itself, which, according to mechanical principles, lead to transpositions of energy of definite extent (this is brought to our knowledge in the various forms of the motion of matter), and gradually to permanent institutions ; that is, with a definite extent of the stimulation, they produce an extent of motion which can be determined in figures. The more numerous are the complexes of protoplasm accumulated, the more complicated become also the visible manifestations of motion and the chemical processes—or, briefly, the reflex processes increase and become more complicated. We subsume under this conception the ordinary reflex movements—*i.e.*, certain purely physical transpositions of the parts in space, and the reflex processes (transpositions taking place reflexly) which concern not only the position of the smallest parts of tissue, of the organic molecules, to one another (*intermolecular* transpositions), but, above

all, the combination of atoms with other atoms—*i.e.*, intramolecular transpositions (of a chemical nature).

To produce a certain reflex activity—*i.e.*, to cause the accumulated, easily transposable energies to perform their work—it is necessary that a certain factor of inertia, which might also be designated as the swelling of stimulation, be first overcome; and the process of causation requires a certain ever so small period of time, because, before energies can be liberated, the resistance of conduction and that of distance must be conquered. In a number of cases there is not merely a process of causation that acts only once, but the stimulation must represent a sum of living force which is at least equivalent to the sum of energy liberated by the organism. In other cases the body, acting as stimulation by special affinity, becomes effective only in that it brings about, *in rapid succession*, causations and transpositions by means of which much greater sums of energy are transformed into labor than correspond to its own living force present in the unit of time.¹ These cases include, for instance, the ferment effects by transmission of oxygen after M. Traube, and also the action of microorganisms which transform exceedingly great sums of energy into work (into lively motion of their own molecules leading to the segmentation of groups of molecules—*i.e.*, producing new individuals). Not in every instance, therefore, is the size of the reaction in direct proportion to the size of the original stimulation—*i.e.*, no sum of energy is produced as work in the organism

¹ Such labor can only be performed, according to the law of the preservation of energy, if the body that displays such effects is enabled by another force (heat) to perform more rapid and more intense intermolecular and intramolecular oscillations, if the same amount of work is not applied to the firmer combinations of its molecules and atoms as in other substances.

which corresponds to the existing primary living energy of the stimulation. For instance, a muscle, upon the formation of which depends the variety of energy produced, performs a great amount of work upon the most insignificant stimulations (sensory stimulation), owing to its connection with the nervous system wherein it is inserted as an apparatus of causation; the muscle, therefore, must have energy stored in a form in which the combination of the energy in molecule and atom is the conceivably weakest, so that the slightest cause produces something like an explosion. It may be stated incidentally that, possibly, in a contraction in which nitrogen is to be transformed, it may be a question whether explosive niter combinations which develop only energy and but little heat are really transposed, whereas there is no such question in febrile processes in which the muscle produces heat (intramolecular performance) but no work (intermolecular performance), combined with alteration of volume. In every instance, however, a stronger stimulation acts in the same individuals, *ceteris paribus*, with marked effect so long as easily producible amounts of energy are on hand. But even if a certain amount of living force is liberated by the production of energy in consequence of stimulation (*i.e.*, by a cause which leads to the saturation of free affinities of the living molecule), it will never become fully manifest as *external*, visible labor, since a part of the energy is naturally transformed into heat and is consumed for internal (intramolecular) processes. Every reaction, therefore, is a transformation of energy into labor and heat.

The sum total of all processes of accommodation is, finally, that, by the acting upon one another of the affini-

ities of all parts of the semisolid organic substance in lower animals, and by the aid of the blood and of the nutritive fluid in higher animals, the performance of essential labor is guaranteed even in all those cases in which the energy can be replaced with difficulty only, or in which suddenly more considerable, greater demands might be made upon the stock on hand of energy, so that, therefore, the individual is preserved under the most varying conditions of its surroundings, and is rendered fit for the perpetuation of its kind. This can be accomplished only in that the perfect protoplasm engine (the individual) performs such a sum of extra-essential work that the amount of energy thus produced always supplies also the living force required by the processes of causation.

Reflex movements and transpositions, therefore, in the course of organic life have so shaped themselves that an alteration of the external stimulations at once either calls forth a different distribution of labor (labor is strengthened in one area, modified in another), or causes all parts simultaneously to perform an increased amount of labor, for the amount of energy on hand usually exceeds the required performance of labor.

There is at hand a sum of *reserve energy*, of rapidly producible elasticity, which, aided by the oxygen inside and outside of the body, alone guarantees the working capacity of the body under various conditions, in that it permits of an extensive increase of the processes of combustion which furnish accelerating energy for the numerous particles, and also, by vicarious activity of organs not directly stimulated, supplies the amount of energy required at the moment to replace the energy consumed. Therefore, the animal organism is also enabled to produce, apart from the labor which only

refers to internal activity with changing stimulations, living force for the processes of causation, to perform labor outside of itself—*i.e.*, with the aid of special machines, the muscles, it can produce movements of bodies outside of its *ego*, and move masses—for instance, its own body—in space. This extra-bodily work, through which the organism furthers its own ends (motion, ingestion of food up to the assimilation of the same), and the work within the body, which the processes of causation produce, represent the sum total of the energy transformed by the organism. Of course, the practical effect furnished by the organized (natural) machine in regard to extra-bodily work, altho it works to greater advantage than any other, is not equal to the sum of energy consumed, since always, as substratum of the living force necessary to preserve the processes of causation (physiological stimulations), a large sum of energy is transformed into heat, which later is lost by transmission; *apparently*, therefore, it is not expressed as work performed. *This heating of the machine, which in artificial machines almost always means a total loss, owing to the better conduction of heat therein than in bodies, serves in organisms for the proper purpose of maintaining a certain temperature for the substance of the machine.* The heat supplied is absolutely necessary to make labor possible, for it accomplishes not only what in the machine means the preliminary heating of the water to be transformed into steam, but it also causes labor to be performed, in that it, above all, enables the numerous particles of the organized substance to shift away from each other; it guarantees greater motility, lessens internal friction, and furnishes the living force to act upon the oxygen of the atmospheric air.

Therefore, in its widest sense, the reaction of the body is the transformation of energy which takes place in consequence of the innate (phylogenetic, physiological) stimulation necessary to the preservation of the organism (growth, nutrition). Secondly, reaction is that measure of transformation of energy which must be converted into labor at each increase and decrease of stimulation, so that the processes of causation and the remaining performances of labor can occur without interruption. The alteration is the stronger, the labor performed and to be performed the greater, the more one and the same process of causation (stimulation) produces conversion of energy into living force—*i.e.*, a loss of energy on hand, for the *combination of energies furnishes heat, and heat developed acts as a new process of causation*. Physiological stimulation represents the measure of stimulation found phylogenetically for the species—*i.e.*, a certain composition of molecule aggregates as the optimum to regulate the quantity of labor under definite external conditions of life. It is the minimum of producing energy, by means of which the sum of energy necessary to the preservation of the individual under adequate conditions of life is converted into extra-bodily labor, and naturally is also the expression of the amount of transformation accomplished. Physiological stimulation, being thus dependent upon external conditions of life, of necessity represents some form of autoregulation. It is bound, in keeping with altered conditions, at once to undergo a definite change which causes complete compensation—*i.e.*, by which, notwithstanding the altered conditions of labor, the sum of living force (in the form of heat) necessary to the full activity of the machine is readily supplied. In short, stimulation

must be what the pendulum is to the clock. Oscillating under the influence of gravity, according to the varying degrees of attraction to which it becomes subject, the pendulum furnishes the power supplied to the wheels of the clock by the spring sometimes more rapidly, sometimes more slowly. Stimulation and reaction, process of causation and bodily labor, therefore, are correlative, from which follows a nearly stable quantity, *the preservation of the individual*. Now, since the different individuals do not represent one and the same quantity, stimulation and reaction must be reciprocal but different quantities in each separate individual of the same species, the determination of which depends upon the individual qualities. This factor is known as predisposition. Predisposition is the faculty of the individual to receive existing energy in consequence of definite stimulations, and to convert them into labor, and it depends upon a property given at the first combination (innate) of the molecules constituting the body or the individual apparatus. It depends upon *the primary stimulability of the protoplasm—i.e., upon the extent of the innate faculty of causation which is identical with the primary (intramolecular) combination of the atoms, and upon the extent of the at all possible transposition of energies, which is identical with the intermolecular power of combination, by which the molecules of different qualities are united into one aggregate of molecules. Predisposition, therefore, depends upon factors which in each individual instance, even from the moment of conception, characterize the vital processes in the tissues of the new individual.* The more easily stimulation can be transmitted from molecule to molecule, the more rapidly and strongly the processes of causation take place even in the ovum, the greater is the phylogenetic,

the physiological stimulation (extent of the process of causation), the larger and the more readily available is the amount of energy in store, the more rapidly and stronger is the reaction—*i.e.*, the predisposition to react. Predisposition is what we call in a combination of galvanic elements external and internal resistance to conduction, or what in explosives constitutes the faculty of furnishing more slowly or more rapidly an enormous amount of labor, shattering the complicated molecule. The various nitro preparations (nitrogen chlorid, potassium chlorate, common gunpowder, etc.) are possessed each of a different predisposition to react—*i.e.*, it requires varying amounts of living force to interrupt the continuity of the sum total of molecules of the explosive substance and to liberate a more or less considerable sum of living force. But since in the organized body (the living molecule) we are dealing with a discharge and recharge—*i.e.*, with replacement of intramolecularly altered, shattered molecules (the charge), by homogeneous molecules, and with reabsorption of the same by constant molecules entertaining only intermolecular relations (the machine proper)—rapid repetition of the discharge is naturally associated with a condition of diminished reaction, for stimulation does not now find the quantity of energy as readily available or in such a composition as to be at once released. Repeated stimulations have called forth a condition of apathy which is probably principally due to the absence of easily convertible substances—*i.e.*, of such as are endowed with strong affinities, and therefore facilitate the conversion into living force; however, it may also be due to the formation of certain constant, intramolecular combinations which in part may manifest themselves even in visible

tissue changes, as in the salivary glands. This condition is variably known as atony, fatigue, paresis. *The period of time, therefore, required to replace energy plays a great part in the definite construction of that quantity which we call stimulability. The latter is the greater the more readily energy can be replaced.* ($St = \frac{E}{T}$, if *St* signifies the capacity for stimulation; *E*, the sum of energy; *T*, the time required to replace the same.)

However, if the stimulations act for some length of time, with the interpolation of proper pauses, the lesser machines of protoplasm, which, until then, had not been used, also become active, and every organ, every muscle always contains a sum of elements not in full work; even those that are active do not, as a rule, exert their functions to the limits of their capacities. Then the active ones also work so much more, so that now the same stimulation causes a greater amount of labor to be performed. *Practise*, therefore, is on the one hand the gradual activity of a greater number of machines of force to the limits of their capacities, and, on the other, the improvement of the supply of fuel, in that the amounts of energy are present in greater quantities and in a form which allows of their immediate utilization in labor—*i.e.*, therefore, the quickest combination of affinities. *Adaptation* is that form of bodily labor modified by practise in which gradually, when the new, more powerful stimulation no longer changes its potency, a condition of stability again becomes manifest in which, therefore, an increased but constant additional production is accomplished. Of course, after it has adapted itself to greater requirements, the organism no longer, or at least not in a form visible to us, reacts to the former small quantities of stimulation. The process of adaptation is naturally

only to a certain degree combined with an alteration of the chemical constituents in that more resistant combinations, with constant stronger binding in the molecule, are formed. However, it is probably clear that the process of adaptation, important as it is to the development, and advantageous to the possibility of the performance of labor of the individual, would lead to a negation of the principal factor of organic life—namely, the capacity for stimulation—if it would develop uniformly in all parts and would gradually increase. If an organism should continue to become less capable of stimulation—*i. e.*, would no longer be capable of producing energy upon maximal stimulations—it would no longer be alive, or, at least, it would be very close to the confines of death; for life means to develop labor from energy by autoregulation (production of processes of causation). An organism lives least during that period during which the least extra-bodily labor is performed (spores, larvæ, chrysalides, ovum previous to fecundation), or, we might say, it shows the least degree of visible labor when it least deserves the designation of a “living organism.” Therefore, we call that condition in which a part is no longer able to perform extra-bodily labor paralysis (in the individual sense). (Such a condition, visible to us, is found only in the apparatus which perform extra-bodily labor, as in the muscles which are separated from their nerves, and in the glands if they do not produce any secretions; for the internal labor of both tissues is the combustion of higher combinations with the development of heat.) *Paralysis in the sense of physical biology is the condition of impossibility to create processes of causation (Auslösungsvorgänge), and to produce energy by them.* Death, then, is that condition of organized matter in

which all processes of causation have come to such a state of rest that they can no longer be put in motion, since the grouping of the atoms in the molecule has become so firm that the liberation of living force would be associated with a destruction of the molecule. This is the condition in which molecular oxygen, with exclusion of bacteria, no longer exerts an influence upon the organic molecule. Putrefaction is that condition in which the organic molecule, with the development of acid, is destroyed only by the action of *living organisms*, which again are endowed with strong reducing affinities.

VIII

CONSTITUTION AND THERAPY

ALTHO it has become old-fashioned to speak of *temperament* and *bodily constitution*, this must not hinder us from acknowledging the fitness and correctness of such designations in a practical respect, for all phases and epochs in the history of therapy are directly or indirectly connected with the conceptions of the constitution resulting from phenomena observed in one or two distinct generations of human beings. The systems of therapeutics, however great in number, however different they appear to be at the first glance, can always be readily reduced to some simple forms by the expert. They are all based upon the fact that, *in the history of the development of mankind, certain peculiarities repeat themselves with tolerable regularity, therefore general therapeutic endeavors, to be efficacious, must adapt themselves to these peculiarities.* Yes, it is safe to say that *these endeavors can be efficacious only so long as they duly consider these peculiarities, and they must become ineffective and be abandoned by their most eager adherents when the characteristic phenomena of life of the generation or generations to which they belong are displaced by the often opposite ones of another generation.* *Bloodletting*, for instance, can find adherents only at a time in which the appearance and the plethoric condition of the patients is an invitation, as it were, for venesection. But all endeavors in this direction must become purposeless, and even lead to

therapeutic failures when a vigorous, robust, plethoric generation is displaced by one of a *nervous-anemic habit*. It is of greatest interest to pursue these changes in the external appearance of man, which, throughout the history of medicine, and in the course of the personal experience of the individual, if it happens to occur at the *turning-point of such periods*, are always followed by a change of all human endeavors and a reversion of all prevailing therapeutic principles, and to study the transition and the resultant mental and physical struggles. Since the average of the mental and physical manifestations of the living generation may be designated as the expression of an epoch, it follows naturally that (as to the European the conception of physical beauty is inseparably associated with the white color of the skin) the constitution also has its share in the determination of the ideal of beauty. Therefore *fashion*, which, after all, *expresses most precisely only some directions of human development, and, consequently, also prevails in hygiene*, sets up requirements as standard which logically result from the prevalent qualities of a generation. What we call fashions of the day are only the arabesques that make due allowances to the necessary alterations of taste, to the craving for change. *The law which manifests itself in fashion, or rather hides itself behind it, is the expression of a certain direction of mental or physical development* which we are bound to follow, since it must, with mechanical precision, lead to the attainment of certain physical or mental conditions. The prevailing fashion through which the natural law manifests itself seems gradually to effect, by means of the corset, certain transformations in the organs of the female body. Women of certain classes, or some of the women of all classes,

are to be qualified to attain another stage of development bearing some relation to the emancipation of woman (possibly being its preliminary condition), and hence the inexorable law compels them to lace the thorax until the new condition of development will have been reached. The fashion of the *day*, always transitory, considers *only the requirements of contrast*; it alters and changes external appearances. But, whether the outer garments are rich in folds, showing actual waste of material, or whether they cling closely to the body, the tight lacing of the body remains the same; in fact, it appears to be most extreme under a blouse with an abundance of folds.

Whereas thirty years ago a florid color of the face, a moderate adipose tissue, wide hips, large muscles, and a good appetite were considered indications of good health, fashion's ideal during the last decades is a pale complexion, a very modicum of adipose tissue, and a slender waist. In accordance with this ideal, fashion also decrees that one heed the requirements of the body in regard to food and drink as little as possible. We actually observe that all endeavors of fashion and even of fashionable therapeutics have followed and still follow in the same direction. Antifat and starvation cures are the order of the day; the mode of living of all classes, especially of those that set fashion, is *in every direction* contrary to the true hygienic requirements for strengthening of the body. All efforts were, and are still, directed at converting the plethoric generation of the past into an anemico-nervous one. Still, in our opinion, this *mutation of periods* is not an *arbitrary* one, but follows the *law of a definite development*, and what we call fashion, command, and law are only the means by which we are

compelled, owing to a mechanical necessity in development, to accomplish what nature requires. *Fashion and custom are but the outer forms and means under which and through which the inexorable law of development is carried into effect.* But since development extends over periods which are far beyond the circle of observation of the individual, we became accustomed to consider as an isolated manifestation what is nothing but one *link* of a *long chain of development*, and we are most apt to lose sight of the connection of the manifestations. Thus it occurs that our laws and commands are still *operative* while the trend of development has already *changed*, and that we attempt to arrest the course of nature by considering as the determining factor not the aim of development, but the outer form under which we observe that this development is carried into effect. We thus insist upon the observation of this outer form, even at a time when a reason for its application has long passed away. *We are not familiar with the direction of the law of development*, and, therefore, with a certain *inertia* we persist in the old direction when a new one has already been adopted. We still heat our conservatories, despite the fact that the sun has been doing its duty for some time. We attempt to *practise medicine after the old method*, altho a *new generation*, arising with new endeavors and new claims, demands *new view-points* and new directions. We seem to forget that the phenomena observed in the human body develop in the course of time, in spite of the apparent homogeneousness of the individuals, upon *entirely different substrata*, and that, altho it is always a question only of a very *limited* circle of forms under which these changes take place, the same phenomena may be due to *entirely different causes*, owing

to the *diversity of the reacting bodies*. A plethoric individual—*i.e.*, one in whom a certain surplus of working capital exists in consequence of innate disposition, accumulates fat because he must live on this surplus in times of starvation. This accumulation of fat is quite as necessary as it is with hibernating animals; it represents a physiological saving. Quite different is the accumulation of fat in the anemic nervous; these either work already with a reduced capital of blood, or they lavish their capital more rapidly. If accumulation of fat becomes manifest in such a subject, it can be due only to the fact that the food ingested is not sufficiently digested, that they either eat too much, or—the usual case—the savings are located in the wrong place. While it is well to encourage a moderate amount of fat development in a certain form of congenital plethora, since it represents a reserve capital, the same condition should be combated in the nervous and in the anemic; not, however, in that food is directly withdrawn, but by preventing an erroneous method of operation which results principally from an absolutely or relatively insufficient supply of oxygen. We shall again refer to this point later on; here our object was simply to show that the apparently uniform manifestations may, with an alteration of the substratum, yet be due to entirely heterogeneous causes.

While it is impossible for us to oppose the tendency of the period—*i.e.*, the definite direction of development, and while we are unable, therefore, to prevent the transition from the plethoric to the anemic *habitus*, still our endeavors should exclusively be to render the transitions of development as little abrupt as possible, and, above all, to limit in time the exaggeration of a certain tendency which corresponds to the law of inertia. We are

able neither to arrest the current of development nor to direct its course according to our limited comprehension, but we can, by *correctly anticipating the phases of development, render the resistance of transition that will become manifest as slight as possible to the new direction.* Much in the development of the individual and in that of entire generations appears abrupt to us, simply because we, endeavoring to persist in the old direction of development, fail to perceive the signs which announce the appearance of a new, often opposite, direction of physical and mental development. We continue, therefore, our attempts to keep the course of development forcibly in the old tracks which have become dear and familiar to us, until occurrences which will take place with mechanical necessity demonstrate to us the near-sightedness of our reasoning and the insufficiency of our actions. Pathological constitutions change in almost regular periods—*i. e.*, the generations of human beings vary in whom the processes occur which we designate as life and disease, and the conditions of existence vary, so that the external manifestations from which we infer the effects of the conditions of life upon the human body are bound to present during a longer period a thoroughly varying picture to the observer. And if at *different periods the same causes have different effects, or if different causes produce the same reaction,* it is obvious that also the *measures* serving to aid the individual in the struggle for existence (many of which are contained in the endeavors which we call hygiene and therapy) are bound to *change*, since what was useful in one generation is either not serviceable or even directly harmful in another, which is at variance with the former in almost all its properties. Hence the physician, no less than the legislator, must

not under all circumstances deduce from the experience of *former* periods a binding form for a *later* one. He must be able to comprehend the signs of the times, in order to judge correctly just when a new direction of development has begun and what course it is taking. And then he will be successful only when he does not force the *old forms* upon new material, but finds for the new material also new forms, or, among those already on hand, at least the forms that are the most suitable.

IX

CARE OF THE MOUTH IN THE SICK

THERE is no dearth of popular and scientific treatises on the care of the cavities of the mouth and of the pharynx in the healthy and in the sick, since daily experience amply teaches us to appreciate the importance of this domain of hygiene. Yet ignorance of the simplest directions or negligence in carrying out the necessary measures generally prevails, creating a great deal of mischief.

It is probably in order, therefore, to dilate upon the causes of the *secondary* affections of the tissues of the oral cavity that develop almost regularly in the course of many disturbances of the general health unless preventive measures are resorted to in time, and it is at the same time proper to state the simple means permitting of an easy *prevention* of such occurrences. It would surely be absolutely wrong to wait for the appearance of manifest signs of such a disorder before instituting treatment, for *prevention of disease* should be the principal aim of physician and nurse. This should be all the more so in this instance, since the development of pathological disturbances in the oral cavity not only in itself signifies a material aggravation of the original disease, but also because more extensive changes of tissue may no longer, as a rule, be removed by simple hygienic measures.

As a danger-signal that announces affection of the

cavity of the mouth, I would name: unusual dryness and deep red color of the tongue and of the mucous membranes of the cheeks and gums or palate, cessation of secretion of saliva and of mucus, and difficulty in swallowing. Further signs are furnished by the swelling of the small follicles of the mucous membrane of the mouth and of the base of the tongue, fetid odor from the mouth, thickly coated tongue and gums, bleeding of the gums, constant tickling in the throat, tendency to retching and vomiting, and obstruction of the nasal cavity. Signs of severe affection are formations of ulcers on the gums, on the tongue, the mucous membrane of the cheeks, the appearance of fungi in the form of white areas upon a deeply reddened basis; finally, swelling of the external glands in the lower jaw.

The conditions that cause these changes in bedridden patients *are those disturbances which affect the normal functions of the body in general or those of the digestive apparatus*, of which the oral cavity forms a part in particular. In other words, any one who is fully conscious, moves readily and has appetite, is less subject to disturbances of the functions of the organs of the mouth than those who are unconscious, paralyzed, suffer from chronic weakness of the digestive organs, or are affected with febrile diseases. Patients who use powerful drugs, such as iodine or mercury,¹ or those who, owing to general

¹ I wish to point out that thus far I have always succeeded in preventing affection of the gums from the use of mercury preparations even in those cases in which a *marked individual irritability* was present, provided, in accord with the old experience, the measures for the treatment of the oral cavity were applied one to two days previous to the employment of the drug and were continued during the entire course of the mercury treatment. Energetic mechanical cleansing and rinsing with mild astringents (bitter) may be aided by (powdered) boric acid, of which a small knife-tipful should be rubbed, two to three times daily, over the outer surface of the gums.

debility, are ordered to use strong alcoholic drinks (wine, brandy), require a careful surveillance, as do also patients with carious teeth, and smokers and chewers of tobacco. (Alcoholic liquors and tobacco smoke, as is well known, irritate the tissue of the mucous membranes particularly, because they withdraw large quantities of water from them.) But *febrile patients*, above all, are exposed to functional disturbances of the mucous membrane of the mouth and pharynx, and careful hygiene of the mouth from the outset is therefore a prime requirement.

The following four factors may be designated as causes of secondary affections in the region of the oral and pharyngeal cavities: (1) Deficient activity of the *mechanical function* of the organs of the mouth. (2) Deficient function of the *glands* and other organs of secretion in the mucous membrane. (3) Lesions of the otherwise normal mucous membrane, which are due to the action of certain *abnormal local causes* (for instance, decayed teeth, which favor the colonization of fungi), or to the absorption of strong irritants; see above. (4) The unfavorable influence exerted upon the vital activity of the tissues of the oral cavity by *general disturbances of nutrition*, and especially by *febrile processes*, the effect of which is manifest even to laymen, in that lips and tongue become absolutely dry.

The condition of the mechanical functions of the organs of the mouth especially deserves particular consideration; for *the act of chewing and grinding of the food in the mouth* is connected not only with a *thorough cleansing of the surface* of all parts that come in contact with the food, but, above all, with a *marked stimulation of the specific secretory activity* of the mucous membrane, upon which again depends to a great extent the nutrition of

the tissue. It should not be forgotten that the activity of the mucous membrane is restricted not only to the function of the glands which serve to secrete mucus and saliva, but it also effects the secretion of certain substances, dissolved and gaseous, which are of importance to the preservation of the organism. Energetic mastication is quite as necessary, therefore, to preserve the working capacity of the tissues of the mucous membrane of the mouth as certain movements of the eyelids (winking, etc.) are essential to the normal condition of the conjunctivæ. The contractions of the muscles of the body in walking and in gymnastic exercises also promote, as is well known, the function of the cutaneous surfaces, the supply of blood and heat, and the secretion of the sweat-glands. In a similar manner should the *rubbing movements* performed *in washing* the body be considered as an especially *important form* of hygienic action affecting the skin.

It will be readily noted that people with otherwise normal condition of the teeth, who partake of a relatively coarse food requiring uncommonly vigorous mechanical action of the organs of the mouth, comparatively rarely suffer from diseases of the mouth, and that, for instance, *fetid breath* occurs only *when the process of chewing has been latent for some length of time*—when, for example, no food has been eaten for some time, as early in the morning. So, too, in toothache—persons suffering from a defective tooth naturally chew on the other side of the mouth—we find that pathological processes of the oral mucous membrane (not caused by injuries or by the direct effect of the affected tooth) are much oftener found upon the unused side. Persons, also, who do not treat their oral mucous membrane in the proper manner, who smoke much, eat their food without regard to its

temperature, and who partake of plenty of strong alcoholic drinks, suffer more frequently from functional disturbances of the organs of the mouth (*e.g.*, fetid odor from the mouth, catarrhal manifestations and ulcerative processes), than those who duly consider the simple directions of oral hygiene. That small children who are still without teeth are often affected with diseases of the mouth, especially during summer, depends, probably, as we wish to state incidentally, not only upon the *great tendency to decompose* of their principal food, milk, but also upon the *lack of energetic activity of the organs of the mouth*, since the work required for the formation and disposition of every bit of solid food is absent in the nursling, and the movements of sucking are not always a sufficient substitute.

As the natural and rational manifestation of the mechanical function of the muscles of mastication is essential to the preservation of healthy oral organs, so also the participation is important of that form of activity of the mucous membrane which we designate as the *faculty of secretion* in its broadest sense. The *activity of the glands*, if the mucous membrane is to functionate normally, must be stimulated in the proper manner; the supply of water and nutrition from within and from without must take place in a sufficient manner—*i.e.*, the *blood* must contain the dissolved substances that are essential to the proper performance of the functions, and the *fluid coming in contact with the mucous membrane* must be of normal quality—not too deficient of water, not too hot or too cold, not too acid or too salty. Attention should also be paid that neither a mechanical irritation of the tissues takes place by unusually pungent and hard substances, nor a chemical one by corrosive or burning

substances. It is essential, above all, *especially to consider* and regulate the supply of water in an organism affected with fever, in order to prevent exsiccation of the tissues—the greatest hindrance to the normal activity of the mucous membrane.

As yet we have not referred to the harmful influence of *bacteria* inhabiting the oral cavity in large numbers, which unquestionably to a great extent cause the decomposition of the contents of the mouth, and in a number of cases give rise to other affections of the oral cavity. It is necessary, therefore, briefly to discuss this point, since, owing to the modern theory of bacteriology, these micro-organisms are, unfortunately, considered to be the *sole* etiological factor, and the conception too exclusively acknowledged to be true that *care of the mouth which does not, above all, consider the extermination of these smallest organisms must necessarily be irrational and a priori ineffective.*

However, according to our opinion, which is probably shared by many experienced practitioners, the harmful effects which are ascribed exclusively to micro-organisms primarily depend upon other circumstances. At any rate, *certain preliminary conditions must be complied with before these enemies can disturb the functions of the tissues*, or, as it is called to-day, can become pathogenic—*i. e.*, change from *external spongers to true parasites, to inhabitants of the tissues proper.*

Well-known simple investigations are sufficient to show that the normal condition and the faculty of function of all structures of the oral cavity, especially of the mucous membrane, are by no means influenced by the presence of a very large number of the most various, also of the so-called pathogenic, forms of bacteria. Bacteria are

harmful in those localities only in which the vital activity of the mucous membrane, owing to some alteration of the functional conditions, has been from the onset permanently and severely damaged in such a manner as to abolish the normal power of resistance to the parasites. This being the case, not only does the slightest lesion create favorable conditions for the entrance of microorganisms, but the bacteria also penetrate the apparently normal surface of the epithelium—which has become loosened, as it were—and reach the deeper layers, finding there chances for accumulation and propagation which are the more unlimited the more the energy of the tissues had already been impaired.

Since the principal condition for the aggressive faculty of the bacteria is the possibility of *undisturbed development*, and since a quiet development is secured only by their *firm adhesion to the mucous membrane, insufficient motion of parts, on the surface of which parasites are lodged, greatly contributes, as mentioned above, to the multiplication and strength of the microbes*, immaterial whether *sufficient exercise of the parts, essential to health*, be prevented by unconsciousness, painfulness upon chewing, a change of the secretory function due to, or manifested by, dryness of the mucous membrane, or some other functional defect of the tissues.

That this circumstance really supplies one of the most frequent causes for the origin of affections of the mouth in persons already diseased can be gathered from the fact that in children, as well as in adults, even simple but strong mechanical action upon the oral mucous membrane will in a certain manner serve as a *substitute for irritation* by the food. For instance, if *chewing and swallowing motions* are produced by frequent *energetic friction*

of the mucous membrane of the cheeks and of the tongue with a moist cloth, causing an increase of the secretion of the mucous membrane and the expulsion of the adherent mucus, it will, in cases that are not advanced too far, usually result in rapid arrest and cure of the developing affection of the mouth. Proliferations of the *oidium albicans* (so-called thrush)—yes, even ulcers—disappear more rapidly and more certainly by the aid of this simple method than by the employment of strong solutions of antiseptic substances. In fact, it is imperative to be very careful with the latter in many cases, since somewhat *strong concentrations* are *directly injurious* whenever the *original pathological process* has already caused a certain *disturbance of nutrition*.

Since, furthermore, an incalculable part of the poisonous substances contained in many of these antiseptic gargles is passed *into* the body (the mucous membrane of the mouth possesses, as is well known, a considerable faculty for absorption, which is not always sufficiently taken into consideration), the employment of such solutions should be avoided as much as possible in patients that are to a certain extent weakened.

Only the consideration of these peculiar conditions furnishes an explanation for the frequent, apparently paradoxical, observation that disturbances of the mucous membrane ascribed to microbes become aggravated particularly after the application of strong antiseptic substances, and that even the fetid odor of the cavity of the mouth and ulcerative and inflammatory processes increase so long as the concentration of the remedy is made stronger. On the other hand, the employment of the mildest agents results in rapid improvement because these exert a favorable influence upon the nutritive con-

ditions of the tissues. However, in judging the effect of antiseptics, which may also be quite advantageous under some circumstances, it is necessary to consider that *two* factors must always be taken into account in this form of treatment—namely, the *real antiseptic power* which causes the *direct extermination* of the germs, and the *mechanical* treatment of the mucous membrane, which is indispensable, and, therefore, is always practised simultaneously, and which, as we have seen, in itself exerts a considerable healing power. It should be further considered, to arrive at a correct estimation of the value of such methods, that an *effective destruction* of the germs can be accomplished for a *short time* only, even with the greatest of care, since every breath draws in new bacteria. We must also remember that a *permanent destruction* of the germs may possibly be directly harmful in that a *certain quantity of the germ contents* of the oral cavity is probably of *great importance for the process of digestion*. There are many reasons for assuming that the germs which are present in the digestive canal contribute materially to the *splitting up* of the *food material* ingested, which is essential to a productive process of digestion, and in this manner play an important part in the course of this process, especially in individuals with enfeebled digestion.

We are in the habit, therefore, in the treatment of diseases of the mouth which may develop in the course of acute or chronic general affections, to abstract entirely from *bactericides—i.e.*, from substances which have the faculty of coagulating albumin or of producing corrosive act on—and to employ simple mechanical cleansing in preference. This method may be essentially enhanced, it is true, by the additional use of finely pulverized sub-

stances possessed of slight antifermentive action, such as boric acid, charcoal, or potassium chlorate, as *powders of this sort combine mechanical with chemical effects*, and, above all, rapidly lead to the removal of the fetid odor due to the decomposition of the contents of the mouth, which is most troublesome to the patient and his surroundings. For the same reason, in cleansing the cavity it is advisable to add to the water (which should be cold and tepid in the case of febrile patients who suffer from chronic affections and have no fever, and whose tongue is strongly coated) small quantities of ethereal substances (peppermint, anis, Cologne water) or of astringent remedies (tincture of myrrh, quassia, calmus), since bitter substances in particular greatly stimulate the activity of the mucous membrane.

The following maxims regarding the care of the oral cavity in disease may be inferred from the above :

(1) Patients with normal digestive function, who are free from fever and are conscious, require no treatment other than that during health.

(2) Patients, especially small children and persons of advanced age, whose appetite is materially diminished, or who partake of nothing but liquid nourishment, *must cleanse their mouth the more carefully the less solid food is taken which requires mastication*. Such patients should gargle several times a day with lukewarm water, to which a little salt or a few drops of tincture of myrrh or Cologne water (see above) should be added, to stimulate the secretion of mucus. In cases in which a tendency to hemorrhages of the gums exists, or in which the teeth are defective, it is advisable to rub, twice a day, a small knife-tipful of powdered boric acid between the lip and the border of the gum.

Patients with artificial teeth should remove them temporarily in case of loss of appetite, or in chronic gastric affections in which solid food is prohibited.

(3) Patients whose sensorium is not quite clear should several times a day be subjected to a careful examination of the cavity of the mouth, as they are very apt to incur small lesions by biting or by pressure of the teeth against the lips. Ulcers arising from such lesions, or from inflammation of the small follicles, are best touched forthwith with powdered boric acid, or with a small quantity of powdered potassium chlorate. The small lesions in the corners of the lips heal readily, as is well known, if they are rubbed off with a clean cloth and touched with boric acid, or rubbed with vaselin.

It is also important, in patients of this category, to wipe teeth and gums and the folds of the mucous membrane every two to three hours (day and night) energetically with a moist cloth, at the same time exerting an *energetic pressure upon the base of the tongue*, so as to produce retching movements, which are able to supplant, in a measure, the normal movements of mastication absent in these cases. Such an irritation of the base of the tongue and of the pharynx not only causes an energetic contraction of all parts of the muscular structure of the pharynx, but it is also conducive to an increase of the activity of all salivary and mucous glands, which is of greatest importance for the flexibility of the parts. Altho the above-described measure suffices in most persons, there are cases in which the irritability is diminished to such an extent that irritation of the base of the tongue does not produce sufficient retching movements, and, therefore, can not contribute to the removal of the viscid mucus adhering to the posterior parts of the

throat. It becomes necessary in these cases to pass directly over the parts of the pharynx with a pledget of cotton attached to a handle, or with a moist feather, and to repeat these measures, according to the severity of the case, morning or evening, or as often as circumstances seem to require it. Patients who breathe with the mouth open should have moist air in their room. It is often also of advantage to reduce the loss of moisture by placing a damp muslin cloth upon the mouth. It is almost always possible in such a manner to prevent the development of an affection of the oral mucous membrane.

(4) In *febrile* patients it is necessary, above all, to look after a plentiful supply of water. Drink should be given to them at least every hour, either cold water or a mildly acid lemonade. The water serves not only to prevent the drying of the parts, but it also assists in stimulating the activity of the glands and in preserving the entire function of the mucous membrane. Unless we are dealing with *incurable* cases in which the patient is still able to swallow without difficulty, it is often possible, difficult as it may appear at the first glance, by means of energetic and intelligent care, within a very short period to bring about the normal condition of the mucous membrane of the mouth, even in a neglected and unconscious patient whose oral mucous membrane and tongue are covered with a thick, brownish-yellow coating, and whose lips are fissured and covered with crusts. It is safe to say, therefore, that, apart from the exceptions mentioned above, *dryness of the oral mucous membrane, marked accumulation of coating in the mouth, or the development of oidium albicans in febrile patients are always signs of insufficient or incapable nursing.* It is by no means sufficient

to *wait* until the patient *demand*s fluid, but drinks should be incessantly administered to him—naturally in the proper manner. He should be coaxed to drink by words, and incited to do so by cleansing and moistening his mouth, and then placing a few drops of fluid upon his tongue by means of a teaspoon. The act of swallowing once being produced, the patient usually will readily take a larger quantity of fluid.

The condition of the *mucous membrane of the lips* should also be especially considered, since exsiccation, which occurs very rapidly at this locality, might, if noticed too late, give rise to deep fissures and ulcerations, and, consequently, to marked disorders.

Many patients are prevented from taking fluids *merely by the sensations of pain* caused at every touch in the dry and fissured mucous membrane of the lips. Swelling of the lymph glands arising in connection with inflammatory processes of the organs of the mouth and throat is also frequently the cause of resistance to the reception of fluids, since it impairs the motion of the jaws and, with it, the opening of the mouth. Children are especially subject to this form of disturbances, and they manifest their irritability distinctly enough, in that they constantly pluck at the dry, itching, and burning lips. It is advisable, therefore, at once to anoint the mucous membranes of the lips of all febrile patients several times a day with vaselin or with lard. Painting the entire oral and pharyngeal cavities with oil, lard, or well-diluted glycerin is also of advantage in cases of long duration.

Any one who has once become familiar with the disturbances of the general health and nutrition occurring in consequence of neglecting the care of the mouth in patients, and who has observed the retardation of conva-

lesence caused thereby, will readily comprehend why we have particularly emphasized the importance of the care of the mouth in general affections, and not only enumerated the usual measures, but also, and above all, explained the reasons for their application.

The nursing of the patient is of greater importance than is generally admitted by the multitude confiding in medicines. It is essential, therefore, that the nursing be *intelligent*, and accommodate itself to the personal conditions which create the importance of the individual case. *There is nothing in nursing that is insignificant and petty*, and nothing is more beneficial to the sufferer than the conviction that his nurse will readily recognize trifling complaints, special desires, and requirements.

X

SOME REMARKS ON INFLUENZA

REGARDING the prognosis of influenza, it seems that it is a very favorable one in our epidemic, and I believe that, in harmony with the observations of the former authors, this result will be arrived at in every instance in which, with a painstaking critical sifting of the material, only those cases are taken as a basis for influenza statistics which manifest the typical character of influenza, all cases being excluded which, occurring with a principally catarrhal character or with severe pulmonary complications, suggest the suspicion that we are dealing with affections which very often also occur at other times during unfavorable seasons—notably in winter—and which so frequently prove fatal to debilitated individuals and to those of advanced age.

That catarrhs and affections of the respiratory tract, croupous pneumonia, delirium tremens, and fatal terminations in general have become extremely frequent does not prove that influenza plays a part in this connection, but it points only to the fact that the noxa which we regard as the cause of influenza is especially favored by, or is only accompanied with, a number of climatic changes which must be regarded as harmful to the well-being of man, especially of those that are subject to the influences of the outside world.

Altho we do not hesitate, as stated above, to consider influenza as a well-characterized epidemic disease, still

we are far from looking upon the infectious character of the malady as being established even with a slight degree of certainty, especially if a *contagium vivum* is assumed to be the cause of the affection without sufficient foundation by means of conclusions from analogy. However, since theoretical deductions in such questions are not conclusive, and since important reasons can naturally also be adduced in favor of an opposite opinion, we wish only to emphasize here that the micro-organism of influenza decidedly requires for its development the cooperation of certain climatological factors which cannot at the present moment, it is true, be precisely outlined. This is sufficiently evidenced by the coincidence of so many affections and the increase in the number of deaths.

The contagiousness of influenza must be *emphatically denied*, according to our experience. If in the face of an almost unprecedented crowding of our hospitals, with partly very insufficient ventilation, and in view of the excessive demands made upon the nurses, a well-defined transmission either from one patient to the other or to any of the nurses had not been observed, communicability of influenza from one individual to the other can only be a very rare occurrence. Two or three cases occurring in the wards among the nurses, which at first incurred the suspicion of being influenza, were, on further observation, recognized as diseases of a different nature (erysipelas), or as not demonstrative, as infection might also have taken place outside of the institution.

XI

THE BACTERIAL ETIOLOGY OF PLEURISY

TO INVESTIGATORS during the last decade bacteriological examination of pleuritic exudates was of chief interest. But it can safely be said that this method of investigation here, as well as elsewhere, has led neither to any conclusion free from objections concerning the pathogenesis of pleuritic affections in general, nor to a positive recognition of the etiology in particular. Neither did the new methods, cultivated with such zeal and allegedly so important for practical purposes, supply any foundations for essential progress in medical judgment and action.

The fact especially demonstrated by all authors, that schizomycetes are absent in the overwhelming majority of cases of sero-fibrinous exudates, speaks more loudly than anything else for the truth *that the presence of microbes can not be identical with the demonstration of the general or special causes of inflammation of the pleura.*

The auxiliary hypothesis that the generators of inflammation can not exist in serous fluid is scarcely sufficient for a satisfactory explanation of the negative bacteriological result. For, firstly, congealed serum is not a bad soil for microbes as a rule, and, secondly, it is admitted that they are frequently found in fluid serum.

Further, suppurative exudates of a non-tuberculous nature always contain micro-organisms (generally even of various kinds), and their presence is not due only to

their transmission by round-cell phagocytes, as proved by the above-named fact that in many cases of serous exudate they are also found to be poor in cells.

To solve these contradictions it becomes necessary to set up a new hypothesis—namely, that the microbes reach the exudate only in those cases in which they are not retained on the interior of the tissue. However, since a very lively intercourse is always present between pleura and its contents, as is shown by the absorption of the most various substances injected into the pleura, the assumption is not very plausible of such an absolute retention in the tissue, the surface elements of which, as is well known, continually desquamate in more marked inflammatory processes.

All these reasons lead us to believe that, besides microbes as the generators of serous and fibrinous exudations, chemical substances or physical irritants of a known or of an unknown nature (heat, cold, the blood mixture) may possibly be active. These irritants, however, in comparison to the pyogenic microbes, should be to a certain extent considered minimal, or they may also be different from them as to quality.

There can be no doubt that micro-organisms play an important part in suppurations, altho not an exclusive and permanent one. It is quite certain that suppuration, the pleura being once predisposed in a definite manner, is maintained quite as much by chemical substances (products of microbes) as by the microbes themselves. The fact that in empyema free from bacteria a free evacuation of the pus is alone sufficient to cause a cure, is at least in favor of the assumption that pus free from bacteria also contains substances which maintain suppuration.

The general results of bacteriological investigation, based upon an article of Jakowski, who utilized as ma-

terial fifty-two cases of his own, and two hundred and fifty from other sources, may be summarized as follows:

(1) Neither in serous nor in purulent and ichorous exudates is it always possible to demonstrate bacteria. However, the negative finding becomes certain only after numerous culture experiments, microscopic examinations, and inoculations.

(2) Serous and suppurative exudates should be considered as tuberculous if no bacteria can be demonstrated.

(3) The majority of idiopathic, non-tuberculous pleurisies are caused by the pneumococcus of Fränkel.

(4) Fränkel's pneumococcus is principally in evidence in metapneumonic and parapneumonic pleurisies; it is often found in association with streptococci and pyococci of the most various forms, also in cases in which no suppuration supervenes. It appears, however, that exudates looked upon as due to mixed infection with more than one species of microbes have a greater tendency to suppuration than the first-named variety.

The microbes of the original disease—tubercle or typhoid bacilli, bacterium coli, etc.—are often found in purulent exudates in association with the so-called generators of pus. Of course, those forms of inflammation must also be regarded as mixed types in which the real pyogenic agent is doubtful. Mention may be made, however, that the demonstration of the pyogenic action of the tubercle and so-called typhoid bacilli has not as yet been made beyond question. *A priori* it may be taken for granted that they, as well as their products, are capable of producing the highest grades of inflammation, provided a favorable tendency is present.

Some authors (Loniga, Pensuti, Fernet) have attempted to prove that a serous pleurisy might also be produced by typhoid bacilli alone, or, more correctly, that exudates developing in the course of typhoid fever contain only the bacilli

which to-day are designated as typhoid bacilli—which, however, had better be designated as a variety of the bacterium *coli commune* developed under special conditions. But since, in the majority of cases, no microbes at all are found in the serous exudate of typhoid fever patients, the probability of the assumption of the above investigators is not very great.

The large, chain-forming, isolated cocci found by Ehrlich in the malignant forms of puerperal fever and regarded by him as a most unfavorable sign, are probably also without the pathognomonic significance ascribed to them.

It follows that serous exudates are by no means characteristically differentiated from all other forms of exudates, for they often contain, even if they do not show any tendency whatever to suppuration, forms of microbes which are considered as specific pyogenic agents. On the other hand, often no micro-organisms are found in empyema, and the pneumococcus of Fränkel is common to serous and purulent exudates.

Microbes are often entirely absent in the empyema of the tuberculous, and the tubercle bacillus is such a rare occurrence that we are in such cases compelled to think either of a mistake in observation, an accidental admixture, or of a communication of a tuberculous focus with the pleura.

Very special precautions should be undertaken in the bacteriological investigation which, according to modern views, is to furnish the principal basis for the prognosis of the case from sputa and pleural exudates that contain only small numbers of tubercle bacilli. This will prevent gross diagnostic errors which might otherwise slip in through some tubercle bacilli, which may have originated from former investigations, remaining upon the glasses or in the staining fluids.

It is difficult to explain the fact of the absence of the tubercle bacilli in tuberculous exudates, and to decide

whether they are fully destroyed amid the number of pyogenic organisms, or whether they continue to exist in the form of nondemonstrable spores—possibly in the cheesy substance of the tuberculously degenerated glands and joints!

The first assumption has not much in its favor, since pyogenic micro-organisms are not encountered, either, in a large number of cases of tuberculous empyema. It is probable, therefore, that the tuberculous exudate is not a very favorable soil at all for the ordinary forms of microbes. Yet, many indications point to the fact that suppuration in these cases is not called forth or maintained by microbes, but by chemical products which, since they can not be fully removed or eliminated by the irritated tissues, maintain a condition of irritation until the evacuation of the entire fluid which contains the main substratum of the irritation causes the advent of normal irritability.

It is well known that injection of pleural exudates into the abdominal cavity of guinea-pigs did not always cause tuberculosis. Culture and inoculation experiments with ingredients of such exudates upon soils especially adapted to the development of tubercle bacilli have also been devoid of any results. It appears that, for instance, sterilized, congealed pleural fluid does not furnish a nutritive soil for tubercle bacilli until about one-half the quantity of veal bouillon with glycerin is added to it before coagulation. At any rate, the bacteriological conduct of the pleuritic exudation and empyema in the tuberculous shows that also the manifold investigations in the domain of development of microbes did not lead to a satisfactory answer to the questions interesting the physician of the relation between tuberculosis and pleuritic processes.

In overestimating the significance of infection as the

most important etiological factor, it was erroneously assumed that puncture, or exploratory puncture, was the principal cause of the introduction of carriers of infection into the pleura. We can not acquiesce to this opinion at all, as such an event is apt to occur even in punctures that are performed with all antiseptic precautions, and, as clinical observation in the past has shown, serous exudates which already contain numerous pus corpuscles rapidly change into purulent exudates even in the entire absence of any extensive operative interference.

It appears certain to us, by reason of long-continued observation, that punctures carried out under the usual precautions can not *contribute to suppuration or putrefaction, in that numerous generators of infection are introduced into the pleura by such measures.* For observations in ascites, on the one hand, show that suppuration of the fluid, or peritoneal inflammation, does not occur even after numerous punctures and under the most unfavorable conditions. On the other hand, it should be considered that the smallest quantities of microbes which might happen to cling to the instrument are bound to be stripped off in the tissue of the puncture canal. Infection by means of the cannula of the syringe, or of the trocar, should be first manifest, therefore, by inflammation of the puncture canal—a very rare occurrence which, if it does take place, may also be caused by subsequent infection of the open canal.

Altho, therefore, we are skeptical regarding the assumption that the infection in punctures is always the cause of suppurations of exudates, still the possibility of harmful effects of mechanical interference does not appear to be entirely out of question under certain circumstances.

We do not wish to deny that puncture and aspiration, as well as a sudden evacuation of the pleura, may occasionally

act as a considerable mechanical irritant, especially if the interference takes place while the tissues are markedly inflamed, or if aspiration is performed too extensively, or is accompanied with frequent shifting of a large trocar. It is surely not impossible that, granted the predisposition to increased reaction, such a maximal mechanical irritation also serves as the process of causation for the especially intense activity of the tissue which we call suppuration.

Carriers of infection are probably always present in ichorous suppuration, being introduced through the lymph channels and by the channels of the pulmonary pleura, or by cells which migrate through the pleura from the lungs. However, the bacteriological etiology is not quite clear in this instance either, as microbes may be absent also in ichorous exudates.

We do not consider a *spontaneous decomposition of a fluid rich in albumin* to be beyond the reach of possibilities, since the preservation of a certain composition of cavity fluids and secretions depends alone upon the conserving influence of the normally functioning tissue of the cavity wall. The conditions in sterilization by highest degrees of heat are surely not identical with the conditions of asepsis in the organism.

The conclusion obtains, therefore, *that bacteriological investigations have failed to clear up the most important questions in the etiology of pleurisy.* For the presence of specific pyogenic organisms, of streptococci and staphylococci of the most varied forms is not necessarily connected with the transformation of the serous exudate into a purulent one, and *the requirements for the formation of pus are as little known to-day as the causes of the various forms of inflammation of the pleura.*

Upon the basis of our experience we must also deny that bacteriological examination of exudates, so extensively practised during the last decades, furnishes any

essential clue for the clinical discernment of the case and especially for prognosis and therapy. We are not inclined, either, with the mere presence of the pneumococcus (A. Fränkel) always to establish a favorable prognosis and to predict spontaneous cure, or to prognosticate absolutely unfavorably if several forms of pyogenic organisms are present, because surgical operations lead rapidly to favorable results even in the most complicated form of suppuration.

The absence of any and all bacteria in a purulent exudate does not safely argue, as some authors would have us believe, the tuberculous nature of the exudate, nor can tuberculosis be excluded, as mentioned above, if tubercle bacilli are absent.

A positive finding of streptococci always excludes the presence of tubercle bacilli, according to Sacaze. However, this author also arrives at the conclusion that the presence of streptococci is by no means determining for the development of a suppurative process.

XII

THE BACTERIOLOGICAL ETIOLOGY OF ENDOCARDITIS¹

EVER since Kreysig first traced a number of changes in the interior of the heart to inflammation of the endocardium, the domain of endocarditis, so important to the physician, has been most minutely studied from clinical, anatomical, and experimental standpoints. This was lately supervened by the endeavor to utilize the results of bacteriology—*i. e.*, therefore, to determine the etiological significance of the various micro-organisms in regard to endocarditis. However, the views of authors concerning the frequency of the occurrence of bacteria in the different forms of the affection are still widely divergent.

Numerous bacteriological and experimental investigations were undertaken to decide this question, resulting in many important disclosures. We took the initiative, some twenty years ago, by severing the central carotid from its first branches, and from there piercing the aortic valves with a probe. These experiments enabled

¹ "Grundriss der Pathologie und Therapie der Herzkrankheiten" [Outlines of the Pathology and Therapy of Diseases of the Heart], p. 147, etc. Berlin and Vienna, 1899. This brief description of the standpoint taken by us for the past twenty years—brief because of lack of space—is a compilation of the following articles: "Ueber artificielle Herzklappenfehler." *Habilitationsschrift*, Breslau, 1878.—*Arch. f. experimentelle Pathol.* Bd. IX.—Eulenburg's *Real-Encyclopädie*, I-III. Aufl., 1882, 1887, 1895. Artikel "Endokarditis"—*Bemerkungen zur Lehre von der Endokarditis*, etc. *Deutsche med. Wochenschr.*, 1887, No. 32, etc.

us to divide all results into three well-characterized groups :

(1) Cases in which it was impossible, in spite of destruction of the valves or tearing of tendon threads, to determine at the autopsies any inflammatory processes, or, more correctly speaking, fibrinous deposits in the neighborhood of the injured parts.

(2) Cases which, altho they presented more or less numerous excrescences of fibrin in the parts operated upon, did not reveal any foreign substances (bacteria), in spite of the most careful microscopical examination.

(3) Cases in which micrococci could be determined, in consequence of the use of imperfectly disinfected instruments, upon the deposits upon the valves of the heart as well as in the embolic foci. These cases showed at the autopsies the exquisite picture of so-called ulcerative endocarditis. This proves the necessity of a distinct separation between *purely mechanical insults of the valves* and *infectious processes* occurring in these parts, as observed in the third category. We believed we were all the more justified in designating these latter as septic processes, as we were compelled to regard the numerous small hemorrhages in the organs, especially in the skin and in the retina, as the expression of a high-graded alteration of the blood, and not merely as a consequence of bacterial emboli. Our later investigations, undertaken according to a better method, have taught us that an accumulation of microbes is the cause of the smallest hemorrhages in the majority of cases, and rarely only a decomposition of the blood (see below). In the other cases, in which the observation of the most scrupulous cleanliness tended to avoid the introduction of infectious

substances, the injured valves represented later on the typical picture of endocarditis.

Wyssokowitsch, a pupil of Orth, subsequently, in eleven cases of benign endocarditis in man, found no micro-organisms in the vegetations, neither microscopically nor in culture experiments, whereas Weichselbaum furnished this proof in both directions in a case of verrucose endocarditis (*streptococcus pyogenes*), so that he, as was previously done by Klebs, Koester, and O. Rosenbach (the latter only for some of the acute, non-malignant endocarditides), determined the mycotic origin of non-ulcerative inflammation of the endocardium. Weichselbaum succeeded also in finding microbes (*streptococcus pyogenes* and *staphylococcus aureus*), microscopically and by culture, in three cases of typically ulcerative endocarditis in the foci existing in the various parts of the body, in the blood, and in the urine; by injection of a suspension into the veins he was able to develop the picture of an ulcerative endocarditis. But the experiment was successful only when previously, according to the method of O. Rosenbach (piercing of the aortic valves), favorable conditions had been established in the tissue of the valves for the absorption and colonization of the invaders. Wyssokowitsch was also able to produce bacterial foci in the valves and in various internal organs by injection of staphylococci and streptococci, after previous lesion of the valves. However, if he injected the above-named organisms in a weak solution or not until several days after the lesion of the valves, no endocarditis was produced; nor did this occur when the microbes were injected in a concentrated form, but from the skin or from the trachea, or when the micrococcus tetragenus, the pneumococcus, or other or-

ganisms that are usually pathogenic, were introduced intravenously. Ribbert attempted to produce myocarditis and endocarditis without direct preceding lesion of the valves. He injected a suspension of potato cultures of the staphylococcus aureus into the aural veins of rabbits, and thereby produced, besides a typical (embolic) myocarditis, frequently a characteristic endocarditis also, which, however, was always localized in the mitral and tricuspid valves, never in the aortic valves. Whereas he at first believed that he could deduce the embolic nature of the processes from these findings, since the staphylococcus aureus had colonized there without lesion of the valves, later experiments caused him to abandon this view. On the other hand, the etiological factor of microbial embolism to explain the occurrence of endocarditis in man has been absolutely established after the convincing investigations of Koester.

The experiments of Ribbert are still, more than those of Weichselbaum and the first ones of Wyssokowitsch, open to the censure that the conditions which he assumed are materially different from those of human pathology; for he employed embolic material of relatively considerable dimensions, and, therefore, he accomplished intense and extensive devastations in all organs, since he accords the most favorable soil to the micro-organisms by the disturbances of nutrition and function caused by his macroscopic emboli, and the most unfavorable conditions for defense to the tissues of the body. *Our experiments*, on the other hand, present the conditions for the study of the disturbances much more clearly, as they show that a general infection can be accomplished by a comparatively slight infection restricted to the valves; for the carriers of infection could adhere only in traces to the instruments which had been previously cleaned but were not correctly disinfected. Therefore, we first created a mycotic

endocarditis and permitted microbiohemia¹ to develop itself, whereas the later observers produced the general infection and left it to chance whether the micro-organisms would also select the destroyed valves as points of colonization, besides other localities. We were able, further, to produce experimentally the picture of pure, non-mycotic endocarditis, and we have placed alongside of the latter the picture of the mycotic variety, with all striking differential points. At the same time we also furnished, altho we have not especially emphasized it, the proof of the importance of individual conditions in the origin of endocarditis, in so far as our experiments showed distinctly that sepsis did not develop in all cases in which instruments were used which were insufficiently disinfected.

That the experimental production of endocarditic affections is favored by a previous lesion of the valves is perfectly in accord with the well-known fact that microbes circulating in the blood colonize preferably at points that are rendered less resistant by a traumatism. This, however, by no means solves the important question of predisposition. Apart from the fact that the least experimental lesion creates disproportionately more mischief than the disorders caused by fever, cardiac weakness, or other agents in the course of an acute disease, and, therefore, apart from the fact that the experiment does not actually produce a predisposition to affection but a direct destruction of tissue—*i. e.*, absolute *death of tissue*—the subject becomes still more complicated in so far as, according to the corresponding results of various observ-

¹ This term is not intended to furnish a prejudice regarding the presence of smallest organisms in the blood proper, but merely to coin a brief designation for the general affection which occurs principally in the blood current, analogous to the former designations, pyemia and septicemia—terms which perhaps some day may come to their own when proof has been adduced that the symptom-complex of the various forms of mycobemia is not so much due to the micro-organisms themselves as to the toxins produced by them.—*Real-Encyclopädie*, II. Auflage, Art. "Endokarditis."

ers, injection of cocci is effective only when it is performed within two days after the lesion. Orth endeavors to explain this by assuming that regeneration and compensation of the nutritive disturbance of the tissue have already set in at this period, as manifested by numerous mitoses of the respective cells. Still, the question remains why, in human pathology, endocarditis occurs, with a perfectly normal heart, within a few days in the course of an infectious disease. Is it really possible that the severe traumatic disturbance of tissue, which, it is true, is performed with antiseptic precautions, has healed sufficiently within two days for infection no longer to take place, whereas in man tissues become affected that previously were perfectly healthy? Is it not much more probable that some flaws are present in the experimental demonstration? Besides, the explanation of Orth considers only the direct secretion of micro-organisms from the blood in contact with the vascular wall, but not the mode of embolus of the vessels of the valvular tissue as urged by Koester. However, the definition of predisposition is not quite exhausted with the recognition of the causes of the mere adherence of active invaders to one part of the organism; the reasons are still lacking why the adhering microbes are capable of entering the tissues. This latter factor is quite as important as the former, since the introduction of the micro-organisms—yes, even their deposition in the tissues—is not accompanied with a direct injury to the organism so long as the energy of the directly affected cells is sufficient to destroy the invading enemy and to eliminate it from the body. The above experiments show also that the injected micro-organisms may colonize at various other localities in which a local predisposition had not been created pre-

viously. Especially the latest investigations of Wysso-kowitsch furnished the interesting result that the bacteria entering the blood adhere most profusely in and between the endothelial cells of the capillary walls of organs with sluggish circulation, showing this to be the battle-field between the cells of the body and the micro-organisms. It may be assumed, therefore, that schizomycetes may also colonize in normal valves, altho the latter, in part probably owing to their deficiency in vessels and on account of their motility, generally offer less chances for the adherence of the invaders.

It follows from the above explanations: *Microbes are the cause* of the affection in the great majority of cases of acute endocarditis, even in those in which a direct proof can no longer be furnished. Typical ulcerative endocarditis, above all, surely owes its origin to a general invasion of microbes. However, there are cases also in which the formation of thrombi, or secretion of fibrin from the blood upon the valves, may be brought about either by mere disturbances of nutrition in the endocardium (owing to fever, altered composition of the blood) or by irritation by products of bacteria, etc., *without the participation of micro-organisms*. This condition may be favored by the mechanical effect of the play of the valves of the heart (to which Kundrat drew attention), in that this produces precipitates—after the manner of beating blood with a glass rod. These precipitates will then form the bases of adherence for the bacteria, cancer cells, etc., circulating in the blood, and in this manner will furnish the favoring factors for the development of malign, mycotic proliferations observed by Kundrat in a number of cases. It is possible, therefore, that here, too, a secondary mycotic infection may take place, creating the

impression of a bacterial cause of the existing changes. Which fungus is the cause of the affection in the individual case can not be determined with certainty. It appears probable that *quite a number of pathogenic organisms* play the part of local generators of inflammation, be it that a primary, a secondary, or a mixed infection is present. It should always be considered in such cases that the absence of micro-organisms in the deposits is often only an apparent one, and is due to the fact that we are probably not yet in possession of the proper methods how to render the specific fungus visible by tinction or how to cultivate it. We believe, therefore, that we are justified in assuming only *one* form of endocarditis which, according to its intensity and extent, and in proportion to the power of resistance of the organism, takes a more or less fulminant course and is accompanied with more or less marked valvular lesions, either leading rapidly to a fatal termination owing to supervening cardiac weakness or to multiple emboli, or is followed, unless full recovery takes place, by a cicatricial contraction of the valvular tissue with more or less well-defined functional disturbances in the valves. It is true, this definition does not include that peculiar form of endocarditis which formerly claimed so much attention—viz., *acute, ulcerative endocarditis*. And, indeed, this form does not belong here, for no affection of the valves of the heart is present in this instance, but a severe *general malady*, the primary cause of which might be a small wound in any part of the body as well as an affection of the valves of the heart. The main characteristic of this infectious disease, wrongly counted among the diseases of the endocardium, is not the, often slight, change of the valves of the heart, but sepsis, or, as we may now term it, *microbiohemia—i.e.*,

a condition of general invasion of the organism by microbes and their products. The valvular affection is only one of the many localizations of the disturbance of nutrition called forth by the blood affection, or the first point of attack of the septic poison. It is not at all astonishing that such a severe process develops so rapidly just in diseases of the valves of the heart, because more favorable conditions for the energetical action and for the easy dissemination of an infecting agent that has entered the blood are not furnished by anything but by a pre-existing pathological change of the valves of the heart. In clinical pictures in which an infecting agent is communicated to the circulation from a local affection, the similarity of the characteristic manifestations, whether the infection is brought about by a lesion of the endocardium or by another wound, is demonstrated by the observations of Litten, who has shown that in infectious processes which arise in any organ—for instance, in the genital apparatus in the parturient—the deceptive picture of so-called ulcerative endocarditis may be present, altho but slight or no changes exist in the endocardium. The main characteristic and the chief danger of this form of disease, therefore, is always the general infection, but not the pathological condition of the valves.

The apparently very plausible objection was raised to this our opinion that then osteomyelitis should not be considered an affection of the bones; however, we do not regard this argument to be very conclusive. It is not our intention at all, as the above objection appears to assume, to eliminate mycotic endocarditis entirely from the category of heart diseases, but only that form in which the local affection either has changed into a general disease or represents only a minimal part of the universal disorder (mycohemias), which then has originated in some remote locality—in a small skin lesion,



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in the lungs, or in the uterus. It would be quite as justifiable to discuss acute miliary tuberculosis under diseases of the heart, because some tubercles may be found in the endocardium, or under diseases of the vertebral column, because a cheesy focus in the vertebral column was the starting-point for the invasion of the tubercle bacilli. Osteomyelitis also belongs into the class of pyemic symptoms if it only represents one of the many localizations of general sepsis.

XIII

CRITICAL REMARKS CONCERNING THE METHOD OF KOCH

PROBABLY never in the history of medical science was the mere announcement of a discovery in the realm of therapy received with such enthusiasm as was the communication of Robert Koch, at the opening session of the International Medical Congress at Berlin, in 1890, stating that he had succeeded in finding a remedy which rendered trial animals immune to the inoculation with tubercle bacilli, and brought the disease to a standstill in animals already affected. The mere rumor that experiments with this remedy had been made on human beings, and had led to favorable results regarding the cure of tubercular diseases, found a hopeful and believing public. With equal faith, physicians and laymen, with but few exceptions, acknowledged as facts the most unlikely curative results, even tho these were directly contradictory to what experience had taught until then. Thus it occurred that the feeling of hopeful expectation rapidly attained, by a peculiar form of epidemic suggestion and autosuggestion, the strength of a conviction, such as is otherwise only based upon proved results, and it is not astonishing, therefore, that, when Koch actually published his experiences regarding the treatment of tuberculosis in man, it seemed as if an ecstasy of joy had seized upon humanity. A new era of human happiness appeared to have been inaugurated, in which the

bugaboo of tuberculosis was deprived of all its terror, and in which the beautiful dream of the curability of all diseases seemed to have become attainable reality—an era which caused the shares of life insurance companies to rise, and which incited some fantastic prophets to ventilate the question what mankind would do in regard to the expected overpopulation of this earth.

And what were the foundations of these Utopian hopes? The following hopeful, but, nevertheless, moderate, sentences of Koch in his fundamental work: "*Weitere Mittheilungen über ein Heilmittel gegen Tuberculose*" (Further Communications Regarding a Remedy Against Tuberculosis):

(1) "Success (in tuberculosis of the glands, bones, and joints) was the same as in lupus; rapid cure in recent and mild cases, slowly progressing improvement in severe cases.

(2) "These experiences lead me to assume that incipient phthisis can surely be cured by this remedy. This may in part also apply to cases that have not advanced too far.

(3) "Statistics are still wanting to show that the cure is a lasting one, for it goes without saying that recurrences are, for the time being, not impossible; however, it may be presumed that they may be cured as readily and as rapidly as the first attack."

Hopeful as these sentences sounded to him also who had the opportunity of observing in the course of years the relatively insignificant results of the therapy of tuberculous diseases of the lungs, still they established certain limits. They caused immeasurably more to be expected from the new method, and accorded a much wider scope to the activity of the physician than was

the case with former modes of treatment. The unquestioned results accomplished by the former modes were not so much due to the active remedial action upon the patients as to the systematically conducted hygienic treatment and to the guarding against harmful influences, whereas the new standard confined the method of cure to rather narrow limits. How will it be possible, then, to explain the exuberant interpretation accorded to the statements of Koch? Quite a series of circumstances are active in this respect, and their enumeration is of importance in forming an opinion in regard to a period which is quite unique, and to events which are without parallel.

The following points must be taken into consideration:

(1) The fascinating name of an investigator who founded exact bacteriology, and who, with every new discovery, however much antagonized at the beginning, enriched knowledge by new facts, was bound, in those *who do not appreciate the difference between demonstration in the laboratory, in the trial animal, and demonstration at the bedside, to call forth the opinion that the investigator who apparently never failed in the above domain, would surely act with the same reliability in the realms of human pathology and therapy*—an opinion, however, which was unfortunately erroneous, in that these *realms are entirely different with entirely different premises of scientific reasoning and of contemplation of observations.*

(2) The joyous astonishment that for the first time a therapeutic method which had arisen upon truly scientific, experimental principles was applied to fully analogous cases of disease, whereas before the objection could be raised to all remedies tested and tried on the animal that pathological conditions produced in the

animal were never identical with what we call disease in man.

(3) The startling fact that the remedy was, at the same time, a means of diagnosis. This naturally opened the door to the fever of speculation and to the passion of establishing, in an apparently scientific manner, truly natural-philosophical hypotheses, and even the bold accusation did not fail to appear that some form of chemical affinity of the remedy to the noxious substances in the body were the cause of the striking phenomena.

(4) *According to the law of contrast*, which also governs therapeutic methods, the minds of physicians and laymen who, until then, were exclusively accustomed to look upon fever as an enemy to be combated with all possible means, were favorably affected by the very paradoxical contention that the onset of fever as a sign of the effect, the beginning, and, at the same time, the most essential tool (if this expression is permissible) of the curative method. The famous saying, "*Credendum, quia absurdum*" (Because something is against the existing opinion and experience), if energetically advocated, still stands the best chances of being recognized.

(5) It should not be forgotten that the majority were strengthened in their belief in the correctness of all—even of the therapeutic—views of Koch by the fact that his statement as to the appearance of a febrile reaction after administration of his remedy was very soon confirmed, thus demonstrating, *ad oculus*, to the dubious ones that a powerful agent was active. This conviction was bound to gain strength when the extraordinarily striking changes of the parts that had been affected by lupus demonstrated in a most unanswerable manner, even to the skeptic, the apparently typical reaction of tubercular tissue. Thus it

was not astonishing that these extraordinary phenomena exerted most fascinating effects upon investigator and observer, and, in combination with the general tendency of generalizing manifestations, as rapidly as possible led to conclusions which could not hold their own if subjected to serious *a priori* criticism, and which under no circumstances corresponded to the strict method of deduction of natural sciences. It was not only that after the employment of the injections changes similar to those on the external skin were believed to be noted everywhere—in the lungs, larynx, kidney, or to be inferred according to the methods of examination practised until then—but the unpardonable mistake was made (in accordance with the old maxim that so often has been a cause of error—*post hoc, ergo propter hoc*) of considering everything that occurred to the patients during or after the use of the injections as the effect of the latter. The consequence was that hyperemia and swelling of the larynx, new focal manifestations in the lungs, cough, increased sputum, etc., were regarded as results of the remedy without ascertaining, by control observations in patients that were not treated, how often these symptoms, believed to be specific in these cases, occurred also in the normal course of the affection, being therefore, as it were, normal manifestations bound to accompany the typical course of the malady. Any one accustomed frequently to examine consumptives of mild or severe types, especially doubtful cases, will not long be uncertain as to the changes of the so-called physical signs over the lungs: how rapidly râles or friction sounds disappear in one place and arise in another, how conditions of dulness and respiratory sounds alter their manner and character, and how also the other local and general symptoms vary, according to

the conditions of the case and to the individuality of the patient.

Any one who brings all these changes into casual relation with a certain remedy, who regards all accidents in the train of the disease, especially the favorable ones, as consequences of the treatment, must not be astonished if the patient or the opponent to a certain line of treatment considers the evil consequences also from the erroneous view-point of causality. Any one who believes a remedy to be very efficacious, and acknowledges its effects only when it leads to favorable results, must not be surprised if others ascribe to it quite as energetic consequences of an unfavorable character. Thus it happened that hemorrhages, intestinal and laryngeal perforations and tubercle eruptions, meningitis, etc.—in short, all changes characteristic of the disease—were regarded as the effects of Koch's treatment, naturally without the shadow of a proof, simply and solely because these events were consecutive to the treatment. And yet our deductions in such cases, if they are to remain scientific, are extremely limited; for we can only claim that, if apparently new eruptions of tubercles are present, the remedy in question (provided it was employed sufficiently long) is not capable of preventing the progress of the disease; but we can never, *since the age of the tubercles can not be estimated*, contend with the slightest claim to conclusive evidence that inflammatory processes or miliary nodules are due to the remedy. Such a claim could be successfully upheld only if all similar manifestations could be excluded with certainty in patients that are not under treatment. However, this is impossible, since at autopsies on consumptives, even in the severest cases, with extensive cavities and caseations, it is always

noted that fresh eruptions can be found in some localities. Engorgements in the brain, in the lungs, hemorrhages into the pleura, rupture of cavities, appearance of pneumothorax and of pyothorax, and similar occurrences, were in a like manner claimed to be effects of tuberculin! And yet daily observation teaches that, in a consumptive who dies with gradually increasing anemia, the more marked stasis manifestations are almost always absent, but that, if he succumbs to an acute aggravation, with a relatively good condition of strength, fresh crops of tubercles and venous hyperemia of the brain and of the lungs with hemorrhages of the pleura are always demonstrable. So, too, high grades of venous hyperemia of the brain and of the lungs are often—yes, probably always—noted in children who rapidly succumb to tuberculous meningitis with severe manifestations of respiratory insufficiency, and it is not to be wondered at if a case of tuberculous meningitis taking a fulminant course under the Koch treatment presents a conspicuous hyperemia of the cranial cavity. Hyperemia and cyanosis are here only the consequences of the respiratory insufficiency, and when the latter is absent, venous stasis will also be wanting, in spite of the treatment after Koch. Thus our cases of tuberculous meningitis that succumbed during the Koch treatment, at the autopsy of the brain showed absolutely no abnormalities of the above category; special manifestations which might have been ascribed to the effect of an agent that greatly influenced the tissues were likewise absent, and also the signs of sure processes of recovery.

As it is impossible to prove in many cases that intestinal ulcers of tuberculous patients are favorably affected by a remedy, so it is also impossible to demonstrate that

the injection has been the cause of a perforation; for we observe, at the necropsies of cases not treated, ulcers in the most various stages of necrosis and clearing up, and yet, as experience teaches, perforation may occur in any form of treatment.

It was necessary to premise these remarks of a general nature, since they clear the situation and permit us to define our standpoint; for those who acknowledge their correctness will agree with us that all *changes which are explicable from the above-mentioned view-point of natural action, and which under every form of treatment are with certainty observed, with an ordinary course of the disease, in a definite number of cases, must not be utilized, pro or con*, so long as a cogent causal connection between them and the therapy is not proved as the *special peculiarity of the case*, and particularly by its *great frequency*, every other reason than the distinct therapeutic interference having been excluded. *A mere coincidence as to time* of an entirely unexpected event with a therapeutic measure does not justify us in construing such a connection.

The real criterion furnished by facts already existing has been entirely lost sight of in judging of the method of Koch, and by no means rare events of daily observation were considered as something never seen and never occurring in the daily course of events. And, further, let this be remembered: it is not in accord with the usual custom that we should gauge according to the method of Koch, well-tried methods, successfully and with certainty employed in deciding as to admission into life insurance and into the army, as to the choice of an occupation and the feasibility of marriage, and at once to cast them aside as misleading and insufficient if the results do not correspond to those of the new method. Quite the contrary, the Koch

method should be measured by the old standard, and by this criterion that rests upon experience we should determine the deeper insight accorded by the new discovery. *It is not incumbent upon us to prove what our old method is capable of accomplishing, for that we know to a nicety; but it must be demonstrated that the method of Koch achieves the same results, or, as some hotspurs will have it, even more.*

Altho the material collected so far of observations concerning the Koch treatment is quite voluminous enough to form a final opinion, simple statistical weighing of the results can not alone be determining; for, as is the nature of such demonstrations, every fact brought forward in favor of a certain maxim can easily be opposed by another fact that proves the contrary. The history of medicine furnishes numerous examples that, by reason of such opposing results, the most contradictory views have been fought out, with equal tenacity upon statistical ground, by friends and opponents of a dogma. If such an unlimited applicability of statistics greatly implicates the determination of clear facts of uncomplicated observation—for instance, of etiological problems—it renders the solution of practico-medical questions still more difficult, and an incontrovertible conclusion can probably not be drawn until after years of observation, when the zeal of the opponents has calmed down, and when all accidental and temporary influences upon the final result will be excluded.

Tho we believe that *empirical investigation has already shown most strikingly to the unbiased that the diagnostic importance of the method is a very limited one, since not really the tuberculous process, but certain factors which are often but not always and principally connected with it, cause the apparent prevalence of the reaction in the tuberculous; and,*

altho we are further convinced that the therapeutic importance of the method in the form as first advocated by Koch, and probably also in the modifications as practised now, is not capable of proof, still, according to what we have just stated, this is also a subjective view which, in spite of our large material of observations, can not claim any greater value in the opinions of many than that of any other scientific observer who is wedded to the opposite view. We must endeavor, therefore, since we can not await the verdict of long years of statistics, to attain our end by some other route—*i.e.*, to arrive at a critical, scientific, objective appreciation of the method. This can be accomplished only along the unobjectionable road of demonstration according to the maxims of natural science. However, the fundamental principles of this method must be made clearer than was the case so far. *General laws, according to which reaction and cure may take place in the organism, must be elucidated in a sober manner. No new law must be proclaimed until its title is demonstrated and the necessity of creating it, since those known up to the present are not sufficient for explanation, or are faulty.* Clinical experiments undertaken with all the required precautions must be utilized to determine whether Koch's remedy in reality possesses the *specific* action ascribed to it, whether it is effective only in its *present composition*—*i.e.*, as the product of tubercle bacilli, and whether it *exercises its influence only by virtue of this specific homologous (O. Rosenbach) attraction to tuberculous, or merely on account of a certain affinity to adjacent healthy, tissues.* So long as these questions are not answered, it is still safe to contend that the apparently healthy who does not react to the remedy may still have hidden tuberculosis, since it is not easy—at least, in the realm of human pathology—to

furnish the only telling proof of the contrary by necropsy, and since the proof is still wanting in the *domain of animal pathology*, and no attempts were made as yet to render the same with sufficient thoroughness. The only other possible objection that the absence of tuberculous processes at the necropsy of individuals who showed a distinct reaction to the injections of tuberculin should be regarded as the resorption of tuberculous tissue enhanced by the remedy, is probably not regarded as worth serious consideration.

It is necessary, above all, to *elucidate the relations between tuberculin and the febrile process in every direction*, and the following questions are still to be answered:

(1) Is the rise of temperature caused by the preparation in any relation to the specific nature, or is this effect possible without it—*i. e.*, would the product of other varieties of bacteria than those inciting the tuberculous process be capable of causing fever in the tuberculous?

(2) Can local manifestations be brought about without rise of the temperature of the body, or are both actions inseparably associated?

(3) Are both actions in causal connection and must one precede the other?

(4) In what causal connection do they stand? For instance, does in lupus the change of the lupous tissue arouse fever, or is it a consequence of the fever; respectively, do both symptoms occur about simultaneously as the consequence of a third change?

It must be considered at the same time that the appearance of local changes, before the thermometer announces a rise of temperature, is not sufficient to demonstrate that the disturbance of the tissue is the primary, and the thermic effect the secondary, event. For it is quite con-

ceivable that the local phenomenon, which is accessible only to the sense of sight, becomes earlier manifest to us merely because the equivalent changes of temperature are not announced in an equally definite manner by our method of measuring heat. There is scarcely room for doubt, according to the previously reported experiments regarding the action of antipyretics, that the influence of the remedy upon the temperature of the body begins quite early. All these questions are still open for solution, and not until after it has been demonstrated that tuberculin affects the tissues even without the connecting link of fever, or that rises of temperature and local reaction are coordinate effects of the remedy; not until after it has been shown that toxins obtained from other micro-organisms, altho they cause fever, still do so only in individuals who are affected by bacteria of the same species; and not until after it has been further shown that they cause a specific reaction only in tissue disturbances due to homologous causes, *remaining ineffective* in others; can the question of the possibility of a specific effect of the preparation used now in tuberculosis (which, however, we deny), either in a diagnostic or in a therapeutic respect, be considered as settled in a positive sense.

Of the questions here propounded, the answering of which alone will be able to furnish positive disclosures regarding the manner of action of Koch's remedy, that one concerning the importance of the febrile rise of temperature has been definitely solved. Neisser (*Ber. der Schles. Gesellschaft für vaterl. Cultur*, 1891), following my proposition, has, by administering doses of antipyrin two to four hours after the injection of tuberculin, succeeded in cutting short the fever in cases of lupus, and yet he observed the local reaction to occur in its full

potency. This confirmed the purely athermic effect of the remedy, which I had already achieved in the injected, and determined that the local irritative action of tuberculin becomes manifest also without the connecting link of the rise of temperature. It is to be hoped that the other objections emphasized by me may also come to a satisfactory solution within a short time. Then only will it be possible to establish a generally accepted theory of the effects of tuberculin.

The second important discussion relates to the fact that, upon the application of Koch's method, and even with the employment of smaller doses, individuals with tuberculous affections unquestionably—*ceteris paribus*—show a normal reaction more frequently than persons in whom tuberculous implications may be excluded to a certainty. According to our opinion, the following deliberations are worthy of consideration in this respect:

The predisposition to become affected by tuberculosis consists in a sum of qualities which we know—for instance, heredity, insufficient development of the thorax, tendency to digestive disturbances, irritability and weakness of cardiac action, and some other qualities with which we are not familiar as yet, among which certain chemical compounds and a certain indolence and weakness of the defensive apparatus of the body surely play a part. Since it must be assumed that tubercle bacilli are everywhere present, but since, according to experience, their preferably favorable development is restricted to those especially predisposed, it is impossible for clinical criticism, in spite of the progress made in the etiology of diseases, to reject the principle of predisposition, for the importance of this conspicuous factor forces itself anew upon every observer, not only in respect to tuberculosis,

but in every epidemic in which, in spite of equal chances of becoming infected, single individuals are alone infected, frequently but one in a numerous family. If the principle of predisposition had not yet been known to us, it could have been inferred from the action of the temperature after tuberculin injections and from the different forms of reaction after the same dose.

One of the two unknown quantities in the equation of disease by an infection, the carrier of infection, is known to-day as to its nature, but, unfortunately, not according to its quantitative relations. If it were so in the individual case, the extent of the predisposition could be inferred from the result. We are in a position to accomplish this, thanks to the investigations of Koch, with reference to the febrile reaction, since we know exactly the potency of the irritation—viz., the injected dose. Experiment, the artificial production of infectious diseases, is not in a position to solve this question, because an important part, possibly the most important one, of the factors constituting predisposition is at once eliminated in that, owing to direct injection into the blood, all defensive apparatus of the body, which otherwise would prevent infection or render it more difficult, are overcome forthwith. If we consider, further, that comparatively enormous quantities of microbes are utilized for the injections, the differences between disease as observed clinically and disease called forth by experiment will be better appreciated. Since tuberculin, according to our own investigations, is without any effect if introduced into the stomach or into the rectum, as it is probably destroyed by the process of digestion, being an albuminous body, we see again that an analogy between the mode of infection by direct introduction of toxic substances into the blood and clinical conditions is incongruous, and we here also encounter an obstacle to the complete recognition of what constitutes predisposition. For even now we are able to measure only that part of the predisposition which I would call the internal one—in contrast to the external one, which protects the body from the absorption of noxious substances

into the blood and tissues; whereas the internal means of defense, which hinder the colonization and development in the blood and in the tissues, depend upon oxydative processes and in part also upon changes of the nutritive soil.

We have frequently observed that individuals who have become tuberculous were possessed of a number of remarkable similarities of their physical qualities, and we conclude, accordingly, that the possession of these qualities predisposes all the more to becoming affected by tuberculosis the more developed and the more numerous they are present in one and the same individual. A person with a paralytic thorax is, as we assume, predisposed to tuberculosis; that he actually becomes affected by the disease is uncertain, and it would be more than bold to establish a positive prognosis in this respect. It appears from experiences gathered from medical observations made in the course of centuries that one of the peculiarities of the tuberculous is their great tendency to become feverish; for the great majority of these patients, even in less pronounced cases, manifest intercurrent slight rises of temperature. However, to consider these elevations of temperature also as a sure sign of tuberculosis, and to conclude from these febrile movements in every individual who is suspected of being tuberculous that the pathological process at the bottom of the condition is in reality tuberculosis and nothing else, is (even if this conclusion be correct in some cases) risky in still more instances, for we know that a hidden suppuration and other affections may also have produced the fever. Since it is a postulate, the correctness of which will not be denied by any one, that fever in infectious diseases is due to the invasion of ptomaines of the generators of the fever, or of toxins in general, into the circulation, we

may safely conclude that, if fever is present in consequence of a pathological process brought about by bacteria, this is caused by an invasion of the products of microbes into the blood current. If a patient afflicted with local foci of bacteria has no fever, we are forced to assume that the quantity of the products is still too small relatively, that the products were prevented by encapsulation from entering the circulation at all, or that the individual in question has a limited predisposition to react feverishly.

If some one shows a marked reaction even after the injection of tuberculin in small doses, so long as it is not demonstrated that such a patient does not have any fever after the injection of other toxins, only that conclusion is permissible that he belongs to the above-mentioned category of patients whose heat-developing apparatus are peculiarly sensitive, and as we know that the tuberculous are the very ones that possess this quality to a remarkable degree, the inference is justified that one so readily and so markedly affected by fever may possibly be also predisposed to tuberculosis—*i. e.*, may be affected already, or will sooner or later become involved. But the conclusion that he now surely is, or is bound to become, tuberculous is illogical; for then we would be obliged inversely to conclude also that any one who has no fever is not tuberculous or is not inclined to the disease. This would be an error which could be instantly refuted, not only from a logical standpoint but also by experience and observation, as we know many consumptives who do not have any fever for a long period, and as fever, after Koch's injections, even in severe bacillary phthisis, either does not occur at all, or only after the employment of large doses (which would cause fever even in healthy

individuals, if they were given as initial doses). To lessen the force of these arguments, founded upon experience, the defenders of the specific action of tuberculin upon tuberculous (homologous) processes maintain that those who do not have any fever are possessed of encapsulated foci not accessible to the tuberculin. This explanation manifests a standpoint that is even more untenable, for here again are logical and actual mistakes. The patient is feverish because the toxins locally produced reach the circulation; he has no fever because the foci are encapsulated; but he is bound to become feverish so soon as they reach there, provided their dose is large enough to affect his heat-regulating apparatus. What occurs in tuberculin injections? Why does the tuberculous patient not become feverish, altho the ptomaines enter the blood in sufficient quantities, and thus all conditions for the development of fever are complied with? The answer must necessarily be: Because the dose is relatively too small. And, indeed, an increased dose invariably creates fever. The patient did not have fever previous to the injections because the quantity of the toxins was too limited, or because his foci were so well closed against the circulation that only small, or relatively small, amounts entered the blood. He becomes feverish at once when his limit of tolerance to the toxin has been determined and the dose is regulated accordingly; only, since it is his predisposition not to be easily subject to fever—*i.e.*, being less irritable—he requires higher doses. To save the theory of the specific action of the remedy, not the only conclusive attempt at defending this view by demonstrating the ineffectiveness of all other toxins is selected, but a special hypothesis is construed which introduces a new axiom known hereto-

fore only in homeopathy—namely, a specific action of the toxins upon the tissues homologically influenced by them (*similia similibus*). This view is thus far supported only by the manifestations in facial lupus; all other theoretical considerations and the observations at the bedside are opposed to it. It is not yet opportune to attempt a full explanation of the condition in lupus. I do not mean to deny that a tissue which is under the influence of an irritant that is well defined qualitatively and quantitatively will more readily respond with a more marked reaction to an increase of this irritant than healthy tissues. However, I wish to emphasize that tissue in the neighborhood of a lupous focus, strictly speaking, is not a normal one, healthy as it may appear; it is in a condition of irritation, of exalted activity, even at some distance from the actual lupous focus, the extent of which we are not really familiar with, and which is unquestionably greater than can be estimated by tactile and visual impressions. The tissue is functionally altered, as brain substance in the neighborhood of a focus of inflammation or softening is in a condition of functional irritation—the remote action of the focus. The processes in lupus may, with due reserve, be explained as follows: into a tissue which, owing to a certain local arrangement of the vessels, is of a peculiar character, and, besides, is in a condition of defense—*i. e.*, of increased irritability—suddenly a considerable quantity of a certain—I do not say specific—irritant is introduced, and this additional marked irritant is conducive to a considerable increase of the local inflammation which naturally affects the functionally irritated tissue to a marked extent. The simultaneously arising fever may be a coordinated event accompanying the intense inflam-

mation, but it may also be—and this is more likely—the expression of the general irritation, of the summation of smallest local inflammations, respectively irritations, which naturally, in those that are predisposed, must accompany the invasion of the circulation by a larger quantity of substances that produce fever. The final effect of such a marked local (and general) inflammatory irritation must manifest itself in necrosis of the inflamed tissue; we note, for instance, that the pus corpuscles in all severe inflammations present a kind of coagulation necrosis. However, a proof that tuberculin exerts a specific effect has not been furnished by the observations reported up to the present; it would be given only when it is demonstrated that other toxins and phlogistic substances do not possess such an effect, and that tuberculin *never* causes a local irritative action in purely inflammatory affections of individuals who are predisposed to reactions, but who are not demonstrably tuberculous.

No proof exists that there is a *difference* between local reaction and general reaction; local reaction, according to experience, is only a *special case* of the general reaction—namely, the expression of a specially increased irritability in certain districts involved in an inflammatory pathological process. It depends upon the general predisposition and upon the more or less favorable conditions under which the remedy is introduced into localities that are especially irritable. It must be left undecided whether the functional increase of the inflammatory processes that were present even before the injection, enhances also, by virtue of certain influences upon the entire organism, a febrile irritation of the tissue of the entire body, which possibly might have been preexisting.

The opinion expressed above is confirmed by the action of tuberculous affections of the skin upon application of the method recommended by pharmacological observers—injection of cantharidin acid salts; local reaction occurs here also in lupus, and, according to some observers, also in the larynx; here, too, with a comparative strength of the dose, and in those that are especially predisposed, marked fever becomes manifest as a sign of the local and general irritation. That the reaction is strongest in the face upon the application of tuberculin, and that a lesser effect can be determined in the larynx—none, according to our observations—depends, as stated above, upon the fact that the skin of the cheeks (feverish flush) and the mucous membrane of the nose and of the mouth are always particularly affected by the action upon the body of any substance productive of fever, owing to certain local peculiarities. This fact does not appear remarkable if we consider that the skin is the principal heat-regulating organ, and that the mucous membranes that exhale water also play an important part in the febrile process. The chief localization of the disease in infectious diseases is likewise found in the external skin and in the mucous membrane of the mouth and pharynx.

Thus we arrive at the following conclusions regarding the effect of Koch's remedy :

The remedy is a *phlogistic* one, and not different from other substances producing inflammation—*i.e.*, it creates in a relatively small dose (the size of the dose is a relative conception, being dependent upon predisposition), an irritation in the body manifesting itself, the higher degrees it attains, in typical inflammation—yes, even suppuration; this irritation is bound to affect all parts

of the body, since it occurs in individuals that are entirely well, and since in the tuberculous, in whom it is particularly marked, it does not, after all, depend upon the seat of the affection. If the extent and the intensity of the local reaction (we mean in this instance not only the reaction of the diseased tissue, but that of all areas affected by the action of the remedy) is especially great, there arises, simultaneously with the disseminated, local reaction which often can not be recognized by our methods, the general reaction, the febrile rise of temperature—*i. e.*, a summation of the processes of irritation causes a measurable elevation of the heat of the body, accompanied, under the action of the remedy, with a destruction of larger quantities of blood, either by the direct effect of the remedy upon the blood, which is unlikely, or by the reactive activity of the cells which require more blood for their increased activity.

But since we know that reaction depends upon a certain predisposition, it is obvious that reaction, and febrile reaction at that, must always occur when the effect of tuberculin has attained a sufficient degree, and this, as is *a priori* clear, must also be the case in the healthy. However, from our observations we have seen that predisposition is not a definite quantity, that it may change, that it may be diminished by habit (vaccination), and that it may, under certain circumstances, be intensified. It follows that there are not only individuals who react more markedly at times, but that there must also be pathological processes and other changes of the life conditions of the organism which intensify irritability, and, hence, the predisposition to react to tuberculin. Now, all these are influences which in themselves act as irritants, and either locally or gener-

ally produce an enhanced functional irritability—conditions, therefore, which in themselves call forth *inflammatory* processes. In pleurisy, in all forms of inflammation which attain higher intensity, and, in that they themselves produce fever, which indicate that the patient is capable of a febrile rise of temperature in response to certain irritants, the introduction of such a potential new irritant is bound to call forth increased reaction, and, therefore, a special rise of temperature. This, however, does not solve the question whether the more marked local reaction, as in lupus, is the cause of the fever. We believe the question may be answered negatively in this direction, for the action of healthy individuals proves that no pathological focus need be present, the increased local irritation of which by tuberculin could be set down as the cause of the fever; the summation of the small local reactions of healthy parts is sufficient to accomplish this. Naturally, the result must become intensified if there exists an increase of the local predisposition to reaction, besides the general faculty of reaction in a circumscribed area, as in inflammatory processes.

If we consider, further, that the disease as such does not represent a *known quantity*, but that in all pathological processes we are dealing with only a *functional disturbance* manifested in greater or lesser changes of all processes of life, it is evident that the form of disturbance, whatever tissues are involved, is merely the expression of the potency of the acting irritation and of the reaction of the organism. Therefore, the extent of each and every new action upon the organism will be determined not only by the form and magnitude of the existing pathogenic agent and by the focal manifesta-

tions of the tissues, but by the functional disturbance, and, above all, by the faculty of the organism to produce an *increased or decreased performance*. For instance, in a patient suffering from severe tuberculosis, whose fever is already very high, a new febrile irritation is often no longer able to produce a further elevation of temperature; therefore, apparently, he will no longer react; in any case, he can not be used for experiments concerning febrile reaction. Thus an equally afflicted patient who never had any fever will often not become feverish upon a new irritation (unless the irritation exceeds the previous ones considerably), just as a healthy individual, according to his capacity for irritation, will or will not show fever, according as he resembles the first-named or the last-named individual in regard to irritability. If it were proved that certain pathological processes intensify the predisposition to react to febrile irritations, an irritant creating fever could be utilized as a diagnostic aid only when these definite processes are at hand. However, it is obvious that not much is gained thereby, for there must exist many diseases and pathogenic agents intensifying the irritability of the temperature-forming apparatus, as we know that *fever is the main symptom of the process in a large number of affections*.

Finally, the following consideration argues against specificity: If there is a question of a diagnostic specific, this would presume a certain relation between the dose of the remedy and the quantity of the tuberculous products; and we would have a right to expect that, within certain limits, the effect will be proportionate to the intensity of the disease. But experience has proved the contrary, for almost unnoticeable affections show a

marked reaction, whereas very extensive diseases manifest none, or but a very insignificant one. *This goes to prove, not that the relation assumed by Koch between tuberculin and tuberculosis exists, but that there is another determining factor, which is predisposition—i.e., the irritability of the individual.*

Whichever way we turn we encounter contradictions and unproved assumptions, and these contradictions are not compensated by practical experience, but instead become still more prominent.

The action of Koch's remedy is, therefore, not a specific, homologous one, effective only in products of the tubercle bacilli, but every remedy *producing locally marked inflammatory irritation* must:

(1) Create fever in those that are predisposed, or, let us say, must create fever if given in a dose that is in a certain relation to the predisposition of the individual, which, therefore, is very variable, and can be ascertained only empirically.

(2) Accomplish this effect even in smallest doses in those that are predisposed.

(3) Produce, in foci that are already inflamed and in their surroundings, a reaction which is all the stronger the more irritated these areas are at the time of the application of the agent causing the fever. The reaction will be considerably more marked if the respective parts are still capable of a special action and have not been exhausted by previous labor. Experience confirms these deductions, for also the salts and the proteins of the pyogenic bacteria in certain doses call forth fever in those predisposed, and produce more marked swelling and reddening in locally inflamed parts.

This characterizes the position which we assume in

regard to the diagnostic and therapeutic considerations that were combined with Koch's remedy. *The remedy can be utilized as a diagnostic aid only in so far as it indicates that an individual possesses a conspicuous irritability to the phlogistic substances obtained from the tubercle bacilli, which irritability is found especially often in the tuberculous, but not exclusively so. Reaction, therefore, does not signify that those in whom it is called forth are tuberculous, but simply that they are more inclined to become feverish than many others. However, this faculty of creating fever does not belong to Koch's preparation on account of its specific property manifested only in tuberculous processes, but it is probably owing to the enormous irritating and pus-producing effect of the remedy in larger doses. It irritates the cells, produces the effects of inflammation, and, in large doses, especially in animals, suppuration, and then, naturally, necrosis as well.*

Two roads are open to us to judge of the *therapeutic value of Koch's method*: One is that of experience; the other, that of critical sifting of the principles of the method. The latter must necessarily lead to a negation of the specificity of the method, and to the conclusion that the foundation of the method of Koch, as well as the explanation Koch gave regarding its mode of action, are entirely insufficient to answer the requirements which may be insisted upon in a new method of healing. Altho, as stated above, many questions are still awaiting solution, and, in spite of the fact that the relation of the phenomena which become manifest upon the injection of tuberculin, has not yet been elucidated and investigated with thorough scientific acuity, the existing experiences and the critical objections based upon them are fully sufficient to show that tuberculin can not be a remedy in

the true sense of the word. It is true, it stimulates the protoplasm and especially the tissues which are in a certain manner functionally irritated, but the proof that this irritation is of advantage is furnished as little as the demonstration that necrosis of the affected tissue takes place under the influence of the remedy. What we designate as necrosis in lupus is merely the consequence of a very marked inflammation and exudation; the tissue does not really become necrotic, but at best only the most superficial layers of the skin, similarly as in the application of cantharidal blisters. It is not probable that the tissues become necrotic—*i. e.*, are killed—directly by the remedy as such; necrosis in this instance is not a direct necrosis of coagulation, as in the administration of chromic acid or of chromate salts in which the epithelia of the kidneys enter a combination with the poison and in that manner naturally undergo a destruction of the protoplasm, but it is a secondary effect of the inflammatory exudation. The markedly reacting cells, saturated with serum, become necrotic as the result of excessive action and saturation of the tissues with round cells (suppuration), but not in consequence of poisoning. The animal experiments which apparently confirm the assumption of a specific process are not unambiguous; they show only the very irritative action of the tuberculin, or of the suspension of tubercle bacilli which produce marked suppuration.

We have just said that it is doubtful whether the irritation of the healthy or already affected tissues produced even by the most minimal doses of tuberculin might be considered advantageous to the patient; in fact, we are inclined to look upon this more developed irritation as a decided disadvantage, for, even tho it is true that a tis-

sue defending itself manifests functional irritation and varying degrees of inflammation, this is no proof that an increased irritation and activity also represents a tendency to heal, the less so since the irritation that stimulates the cells to increased activity is a new one. Not the inflammatory reaction signifies the tendency to heal, but certain processes in the cell that often run their course with manifestations of inflammation. Inflammation is only a secondary process; to incite the same will promote the efforts at healing quite as little as the generation of smoke answers the efforts of those that need fire, altho it is well known that smoke is generally developed when there is a fire. If the most marked functional irritation were a tendency to heal, all we would have to do in every instance would be to add a more pronounced inflammation to the existing one; but we see in all forms of inflammation that nothing is more futile than this endeavor. This error is most strikingly manifest, for instance, in the treatment for gonorrhoea, in which the employment of markedly irritating substances usually does not produce a cure but an intensification of the original affection. To usher in a cure means in such cases just the avoidance of every fresh irritation, and the attenuation of the irritation forming the etiological substratum.

The Koch method grew from a wrong application of the principle of vaccination, in which, as is well known, small quantities of a homologous substance so influence the healthy cell that the invasion of certain micro-organisms furnishing similar substances becomes harmless, because, as it is alleged, they no longer find an appropriate nutritive soil in the affected organism, either from the fact that combinations are encountered here which they were intended to form at the termination of their process of life, and the development of which from the

animal cell is inseparably associated with their own development, or because the cells irritated by the vaccine, owing to this irritation, are in an improved condition of defense, the nature of which is as yet not known to us (reaction). If we should succeed in producing such an effect with definite doses of tuberculin, then, of course, the further advance of the tubercle bacilli would be limited, and the method be scientifically justified. The following deliberation is in order, in view of this deduction:

(1) *The Koch preparation* is by no means a pure, *specific substance*, for it is probable that the preparation called tuberculin which, as is well known, is obtained by sterilization by heat, contains only a small portion of the products to be designated as toxins in the widest sense.

(2) *It is certain that a series of toxalbumins is absent*, so that possibly a substance is employed which must be considered as truly *pyogenic*, solely in the strongest concentration.

(3) *The marked febrile reaction* is certainly *not an advantage*; it should be avoided, therefore, and the dose reduced to a minimum, for the real purpose, the *strengthening of the organism*, is not attained when such high degree of irritation, or inflammation, is produced.

The production of a marked inflammation can be regarded as advantageous only when the *principle of vaccination is set aside*, and we are intent upon producing necrosis at any price to cause exfoliation of the tissue infiltrated with bacilli. However, the tendency of this therapy must be opposed, for the *sequestration of healthy tissue does not usher in a cure*, as Koch believes, but a road is opened up that is more favorable for the dissemination of the colonies of bacilli; only vital, thoroughly healthy tissue is capable

of furnishing a barrier against the propagation of infection.

That no bacilli can be found in areas with extensive tissue necrosis is no proof that it is proper to produce this necrosis artificially. This would be in order only if we could succeed in expelling all pathological matter with the necrosed tissue. Such a process, however, can not be accomplished by means of the internal administration of a remedy, or, rather, without *severe injury* to the organism—at least, so long as medicaments have no *elective action* and will kill only *diseased tissues*. The axiom, "*Quod medicina non sanat, ferrum vel ignis sanat,*" is valid only for local applications to non-vital parts. We have seen at the incipiency of antiseptis that *cauterization of the tissue* with overstrong concentrations of the antiseptics (carbolic acid) acts especially favorably upon the progress of microbes through the destroyed tissue. Now if the spontaneous exfoliation of an invading noxa be favorable, in this instance artificial exfoliation is thoroughly harmful, for, while the former is brought about by the healthy tissue separating itself from the affected parts in such a manner as to sharply define the demarcation between the necrotic area and the healthy one, the former of which liquifies at the borders, and the latter of which is conserved with greatest care, only the healthy tissue should exfoliate, according to Koch.

The fact that a remedy does not exterminate the bacilli does not, *a priori*, argue against its efficacy; on the contrary, we believe we are justified in assuming that a remedy which is a direct bactericide would bring to bear not only an ineffective, but an actually *harmful*, principle. It is safe to assume that an agent which destroys microbes (an antiseptic) is bound to act most deleteri-

ously upon the much more sensitive tissues of the body; and by reason of reported facts we do not doubt that it causes the greatest mischief in the organism and actually promotes the work of the microbes. Nor should it be forgotten that an *effective* remedy is required only to render the vital conditions for the development of the micro-organisms as uncomfortable as possible, in that it alters the nutritive soil, as it were, and very weak concentrations are sufficient to accomplish this. Thus we have shown that quinine, undoubtedly a truly specific remedy against the microbes of malaria, does not directly effect the destruction of the parasites, for the plasmodia continue to be actively motile under the microscope, in spite of the addition of a *concentrated solution of quinine*.

If critical contemplation thus teaches that the principles of Koch's treatment are not correct, that the constitution of the remedy is no guarantee for the fulfilment of the theoretical postulates, bedside experience, in harmony with the above, has already shown that real curative successes in affections of the lungs, which could be ascribed solely to the new method, have not been accomplished with Koch's method. Do not let it be said that patients were improved, that dulness and râles were made to disappear, that normal respiratory sounds took the place of infiltration phenomena, that the sputum had diminished or had ceased entirely, after tubercle bacilli had been previously made to disappear under various forms of degeneration. These apparent successes should not be enumerated, for they can be frequently observed in every method and in quite indifferent treatment; in fact, such results may be brought about even by the mere sojourn in a hospital, or by rest and care, and by abstaining from exhausting professional duties. Quite

remarkable results can be accomplished in a great number of cases if patients come under treatment who are well nourished and who are affected with only slight apical catarrh. We have known for a long time that tuberculosis, which formerly was considered incurable, is improved, comes to a standstill, or is even entirely cured, in quite a remarkable percentage of cases. Why, then, attribute to the method of Koch what we observe to occur also in other conditions, and by no means rarely?

If from our standpoint we do not consider it demonstrated that the results of cure in tuberculosis of the lungs are to be ascribed to the method of Koch, we regret that we are not able, according to our observations, to add any positive statements to the reports of other investigators regarding the cure of laryngeal affections of a tuberculous nature or with reference to the cure of tuberculous affections of other mucous membranes. The injection of tuberculin did not furnish unquestionable results either in rectal fistules, or intestinal ulcers, or in affections of the nasal mucous membrane; nor do our experiences in a number of bone and joint diseases justify us in recommending the method of Koch in any particular manner, and in looking upon it as superior to other methods.

It appears that only in lupus of the face better results were accomplished. I say "appears" knowingly, as definite cures have been rarely reported as yet, and the success of the remedy was manifest mostly only in a more or less distinct change of the infiltration phenomena. Paling of previously reddened areas of the skin, exfoliation of prominences, smoothing of the thickened and desquamating skin, are the most prominent criteria which we are inclined to consider as the signs of a favorable

action of the remedy and of a distinct improvement of the affection. And even with these sparse, really negative, results, recurrences have been determined in quite a number of cases, and in these the hope for the same energetic topical effect as in the first stage of treatment must be abandoned, since the patients no longer react locally as before to large doses.

If we reflect, further, that even the most enthusiastic adherents of the curative action of tuberculin begin to combine injection with local measures, with surgical interferences and medicinal applications (iodoform, pyrogallic acid)—measures, therefore, which even alone were frequently considered remarkable methods of cure (I mention only iodoform, which for a long time was regarded a specific against tuberculosis of the bones, glands, etc.)—we must arrive at the conclusion that the specific curative action of tuberculin can not be of much account.

Little as the favorable manifestations in the symptom-complex of the disease occurring in the course of the treatment after Koch can be regarded as unquestionable effects of the remedy, quite so little is it permissible to look upon all untoward changes as being consequences of the method. We have repeatedly called attention to errors brought about by attempts to construe a *causal connection* when there is present only a synchronous occurrence of events which are in no relation to each other. It can not be denied that the remedy in the hands of a careless person may have injurious effects; these have been enumerated with careful critical sifting when specifying the reaction phenomena, for an impartial conception of the processes is indispensable there also.

We have previously called special attention to the fact

that albuminuria, hemoglobinuria, urobilinuria, and excretion of brown pigment occurring after the injections were not the results of an irritation of the kidneys, but the effects of too large doses of the remedy upon the blood or the hematopoietic organs, and that such accidents, which occur also in the administration of other really curative drugs—salicylic acid, antipyrin, pyrogallic acid, etc.—can be positively avoided if the individual predisposition of the patient is tested first. Smallest doses should be given at first; these should be gradually increased, and at least two days employed for an exact test of the febrile reaction (it might be a question of a late reaction occurring only a day after the injection), the patient being always allowed an opportunity to recover from the effects of the injection. One of the most essential precautions consists in making allowance for every complaint of the patient after the administration of the remedy, provided it is in any form well founded, to the extent that the next dose is not raised, even if no *febrile* reaction has taken place. Especially are nausea and inclination to vomit signs that the patient can not endure the remedy. With such precautions we shall succeed in keeping the patient entirely free from fever and in avoiding thereby emaciation of the patient, one of the disagreeable effects of the method resulting from the unfounded requirement of Koch always to produce a febrile reaction. Great as was the loss of weight in those who were treated exactly according to the first statements of Koch, little untoward effects did the treatment have upon the general condition of the patients when but small doses were employed at first, and moderate increases resorted to only after febrile temperatures were no longer in evidence.

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Regarding the other occurrences, *wrongly* regarded as *consequences* of Koch's method, such as pulmonary hemorrhages, meningitis, pneumothorax, intestinal perforations, miliary eruptions, we have exhaustively expressed our opinion in the introduction.

To sum up, let us say that the evil consequences observed after the injections of tuberculin were not the *real consequences of the remedy, but effects of the wrong use of the same*—a fact often observed with other really valuable remedies of our pharmacopœia in reckless hands, especially when a newly recommended remedy has *not yet been thoroughly tested* as to its properties. The part which predisposition must play in determining the dose is frequently forgotten, and highest doses are employed until the occurrence of evil consequences forcibly illustrates the value of an individualizing therapy.

XIV

THE KOCH METHOD, PROTECTIVE INOCULATION, AND THE LAWS OF SCIENTIFIC, CLINICAL INVESTIGATION

THE Koch method (namely, the employment of the bacterial product called tuberculin for diagnostic and therapeutic purposes, upon the basis of the principles established by Robert Koch, together with a number of other methods—already in vogue—of preventive or curative immunization with bacterial products) resulted from the following view :

The activity of the microbes in the animal body or on artificial culture media furnishes products of metabolism which are accumulated either in the substance of the microbes or in the substratum of the culture medium, and, properly isolated and prepared, are claimed to render an animal body which is threatened or already infected by the same species of microbes, and into which they are incorporated by inoculation (injection), absolutely unsuitable as a nutritive soil for that particular form of parasites. These inoculation substances, therefore, are supposed to render the still healthy body absolutely immune, and to cause one already involved, in a relatively short time, to be freed surely from the invaders. Common to all these more recent methods of protective inoculation is the view that the results of the animal experiment can without hesitation be applied to

the complicated conditions of the affected human organism, and that the observations on animals artificially flooded with microbes from virulent cultures may be placed on an equal footing with the conditions of "disease"—*i.e.*, with processes which develop in the living organism in a "natural" manner, as it were, *after overcoming a number of protective measures and with the observation of a certain period of latency of the pathogenic agent* (the stage of incubation). Common to all these methods—to emphasize the point once more—is the analogization of the experiments in the animal organism with the development of disease in the human body following definite, partly well-investigated laws; all these methods proclaim the identity of *injection* disease with *infection* disease, to use a crisp phrase which probably elucidates sufficiently the principal difference of the conditions in both instances. Compare, for instance, the entirety of the phenomena of the disease which we call diphtheria with the manifestations of the injection disease produced by the incorporation of cultures of the Löffler bacillus, and it will scarcely be possible to speak of an even approximate similarity of both processes.

The new features of Koch's points are :

(1) That upon the basis of theoretical considerations, apparently proved by experiment, he attempts to cure also a *chronic* disease by means of certain bacterial *products* (we shall presently define this term more precisely), whereas, so far, attempts at cure after the principle of immunization were really only made in the so-called infectious diseases, which probably also include hydrophobia.

(2) That he ascribes also a *diagnostic* value to the substance employed by him, and therefore expects of tuber-

culin what I have designated a *homologous* action—*i. e.*, a marked reaction of the body *only* in those organisms in which the tissues are already under the influence of the products of the tubercle bacilli.

(3) That he sees an essential factor for the possibility of the occurrence of cure in the intensity of the irritative effect—*i. e.*, of the local and especially of the *general-febrile* reaction appearing after the introduction of his remedy.

(4) That he derives the curative action of tuberculin from a specific necrosis of the tissues adjacent to the tuberculous foci—from a necrosis which, just because, according to his opinion, it can not be produced in the healthy, should therefore be characteristic of the effect of the homologous bacterial product upon specifically affected tissue.

(5) That tuberculin is not a *toxalbumin*, therefore not a member of the group of bodies which until then were solely employed in all attempts at immunization, but a bacterial protein, one of the substances which so far were really never used in any remarkable experiments.

What position was the thinking physician to take toward the new method—not only toward the continuously repeated attempts of an immediate application of experimental views to human pathology, but in particular toward the *claim of Koch for the immediate practical utilization of his results* in therapy of man? Would, in particular, the clinician, the hospital physician, be justified in rejecting any trial of the new method simply because it was a new one, and because, if we except the treatment of hydrophobia after Pasteur, with its contradictory results, no attempt has ever been made to cure already existing

diseases (or affections the long incubation period of which suggested the long-continued action of microbes in the interior of the organism previous to the occurrence of manifest symptoms) by the inoculation method? Was it permissible to condemn the method if for no other reason than because it was recommended merely upon the basis of animal experiments and upon theoretical deliberations, or because the composition and preparation of the remedy were shrouded in mystery? We are of the opinion that all these considerations were not sufficient to prevent immediate methodical trials of the Koch remedy, for, first, we were reasonably certain that we were dealing with a bacterial product, and a protein at that, since, according to the directions of Koch, the solutions could be heated to the boiling-point for sterilization; secondly, remedies have often played a rôle in medicine without their composition or the theory of their action being known; and, thirdly, it must be considered that an investigator of great merits, even if he deems it advisable to publish only fragmentary, experimental foundations, is fully conscious of the range of his propositions, and shoulders, as it were, the responsibility for his statements and for the relative harmlessness of his remedy. In this respect Koch had done more than his duty, in that he had experimented on himself with an extraordinarily high dose (0.25 gm.), and without having accustomed himself to the use of the remedy. Accordingly, all institutions that had the opportunity for careful observation at once expressed their willingness to investigate the efficacy of the remedy, provided patients would consent to this mode of treatment, and this consent was most readily given. However, this outspoken willingness to experiment on the sick and on the well who offered them-

selves for trials constituted the limit of what was permissible and necessary in meeting Koch half way. *For the physician must never forget that he undertakes far-reaching experiments, boundless in their results, on the most costly material, and he must never, trusting in experimental investigation, even if a prominent investigator guarantees them, go so far that he at once regards results obtained on the basis of animal experiments as irrefutable, instead of taking them not only as starting-point, but as a guide for his own actions.* His trust in such observations must never extend so far that he at once disregards his own well-founded opinion, formed in the course of years upon the basis of his own experience and that of others, blindly to accept new doctrines, burning his old idols in fanatical zeal to exalt the new ones even before they have given any actual proof of their really *superior* value. The responsible activity of the physician, whose highest aim is the healing of suffering humanity, consists, above all, in that he does not, in this laudable endeavor, neglect the *first important principal: not to injure the patient.* His greatest glory must be that he, with prudent criticism and upon the basis of real knowledge of the nature of the laws governing the healthy and diseased organism, gives timely and emphatical warning of the treacherous nature of analogies so easily created by laboratory experiment, with its uncertain and arbitrary premises. He must not, like an *enthusiast of fashion*, be ready, in the presence of new views, even if they confront him in the lime-light of experimental facts, at once to discard the familiar standard of old and tried knowledge. It can never be a question for a physician who, in secure, well-acquired possession of our quite acute and reliable diagnostic expedients, is justly accustomed to attribute a gratifying degree of

reliability to his judgment of the prevailing condition of certain organs of the human body, *suddenly to set aside such views as insufficient, and to gauge by new, as yet untried, theories, the correctness of old ones which have often enough stood the test—for a goodly share of our most valuable social institutions is founded upon their efficiency and trustworthiness.* The physician who has studied the course of a disease in hundreds of cases, who knows the full significance of anatomical changes which can, after all, develop only from severe, long-lasting functional changes, should not believe in the possibility of the miraculous cure of *all* cases, and in the possibility of restitution of completely destroyed tissue, just as if disease were only a parasite or an enemy to be driven from its *hiding-place* in order to leave the *organism intact.*

If it was imperative to experiment with Koch's remedy, the employment at the bedside should at least never have been carried out according to the principles of Koch; for whatever opinion we may have regarding fever, this much is certain: that the *production of fever has never been an aim of the practise of medicine—indeed, according to the condition of affairs, never could be.* It is further certain that no fact can be adduced which would prove that the *causation or the development of fever ever exercised a sure healing effect.* Little as it can be denied that the occurrence of a rise of temperature is a necessary consequence or accompanying phenomenon of certain changes in the body which constitute the essence of the pathological process which we call fever, quite as little is the view justified that for the same reason the artificial production of a rise of temperature should exert a favorable effect upon the course of the processes. The first sign of critical prudence, therefore, should have been to

reject the requirement of Koch that a *febrile reaction was a sine qua non*, and not to take it into consideration, but to begin treatment with the smallest possible doses. Quite as essential was the preservation of the most sober, skeptical standpoint of observation (as remote from opposition on principle as from fanatical acceptance), from which the manifestations arising after the employment of the method should be simply *registered* instead of immediately *commented upon* and *expounded in accord with the views of Koch*. Here it should have become manifest that a physician who sincerely desires the appearance of a remedy must not, for this reason, abandon the rôle of a sober, unbiased observer. It was wrong to behold most distinct signs of cure at the very beginning of the employment of the remedy in cases in which only inflammation was present. It should not have been believed that redness and swelling existed when no changes were demonstrable at all, or when the changes at hand in the physical condition were merely the expression of an every-day feature in the course of the affection, and not the effect of the method that happened to be employed. In short, it was wrong to proclaim, either in the living or in the dead, the *most ordinary* phenomena as something quite *strange or unexpected*, and *rarer ones*, which still are not *infrequent*, as sure effects of the method employed. Sequestrations of tissue, the occurrence of which Koch, in accordance with his theory, had represented as possible or likely, and hemorrhages, which are as frequent in the course of phthisis as changes of the physical signs (which may appear quite unexpectedly from one day to the other—yes, in the course of a few hours), were regarded as the effects of the remedy. Every aggravation of the process, or complications, such as tuberculous meningitis, etc., were

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considered as a propagation of bacilli under the influence of the remedy. It appeared as if an epidemic of suggestion and delusion of opinion became prevalent all over, for old and well-known phenomena seemed to be new and mysterious. Astonishment and triumph at the rapid improvement were quite as frequent at the beginning of the treatment as amazement at the aggravation of the condition in patients treated after the method of Koch. Even the most expert diagnosticians lost that precision and certainty with which they had learned, in the course of years, to utilize manifestations determined by exact observations as a basis for their medical decision. Any one who appeared to be the picture of health, and who, according to the physical findings, was most likely to be perfectly healthy, but who had fever after injections of tuberculin, could not be freed of the suspicion that he harbored a hidden tuberculous focus. Any one who was suspected of being tuberculous without furnishing sufficient data was regarded as a pronounced consumptive because he reacted. Individuals unquestionably affected with tuberculosis were, if reaction failed to appear, vouchsafed the comforting certainty that their tuberculous foci were separated from the body by a solid barrier, or that the tubercle bacilli were already extinct.

And yet here too the method of observation and the only true road of deduction was clearly and simply defined for him who, under the influence of the new theory, was still capable of sober observation. So soon as it was once established that healthy individuals reacted, even tho apparently only after large doses, the diagnostic value of the remedy could no longer be considered conclusive, for since a "healthy" and a "tuberculous" individual, or "health" and "tuberculosis," do not rep-

resent known quantities, there must necessarily be transitions between these two conditions—*i.e.*, cases in which a consumptive with slight irritability does not yet react with the same dose, whereas a healthy individual with greater irritability already shows more or less reaction. But the diagnostic value of the remedy was assuredly questioned when a *tuberculous patient*, in whose sputum tubercle bacilli could be demonstrated, did not react at all; for this went to show that *relations other than the mere presence of tubercle bacilli, or of their products, existed between reaction and reacting organism*. The only possible objection, that the absence of reaction in undoubtedly tuberculous subjects was due to successful autoinoculation of the organism with products of the tubercle bacilli, that the body, so to speak, had immunized itself, is readily refuted by the fact that such non-reacting patients are by no means protected from a further progress of the disease. But if the process is progressive, it is then proved that lack of capacity for reaction after injections of tuberculin and immunity to the action of tubercle bacilli are by no means identical conceptions. The fact, also, that after a very limited time, when cure could not yet have been effected, there could be noted a failure of the reaction to appear—*i.e.*, that there was inurement to the injection—pointed with absolute certainty to the truth that the *reaction could not possibly be due to the presence of bacilli or their products, but to certain individual physical qualities of an unknown nature*, which are found perhaps more frequently only in individuals who have a tendency to tuberculosis, or who are already affected by the disease. If patients, therefore, who suffered from severe inflammatory disorders, with exclusion of tuberculous affections, showed reaction uncommonly

often (as was shown even by the first observations), it was unjustifiable at once to conclude, precipitately and with *rejection of all conclusions founded upon experience*, that the case were complicated by a non-diagnosticated, and with the present methods undiagnosticable, tuberculosis, but it should have been inferred solely and exclusively that the *already inflamed tissue was more irritable, hence more capable of reaction, than the healthy one*, and, therefore, was bound to show more marked phenomena upon the introduction of a new irritant, upon a summation of irritations.

Unfortunately, only a few of these postulates of criticism were complied with, and if, nevertheless, a generally clear conception of the new method was disseminated within a comparatively short time, this was not due to the method of investigation, which, at least during the first months, as explained above, at first in precipitate enthusiasm, then in partial explanation of the facts—the latter at the beginning on the part of the adherents, but soon afterward also on the part of the opponents—did all in its power to distort the truth; but the force of facts itself permitted calmer judgment to prevail. That the method of Koch soon lost all recognition as an infallible diagnostic and therapeutic remedy was exclusively due to the facts that observation was piled upon observation, and a material accumulated which never before had been collaborated in such enormous quantities within so short a period of time; that even among the laity exuberant hopes that all sufferers were bound to recover were soon displaced by a soberer consideration of the many deaths due to the treatment; and possibly also that febrile attacks, occurring under the influence of the orthodox treatment, were observed to affect

the condition of the patient most unfavorably. I say the "method of Koch," for Koch's remedy still finds adherents, tho in decreasing numbers, but they employ the remedy, as should have been done at the very beginning, in minimal doses, without the intention of producing fever of reaction; they use the very smallest doses just because they mean to avoid fever entirely, and they do not expect rapid cure from an exfoliation of tuberculous tissue caused by the remedy, but they consider tuberculin merely as seconding the natural process of healing.

The question would be in order here why once more we enlarge upon the epicrisis of an event which in our rapidly moving time is far behind us, and which, after a brief period of error, has at last terminated in victory for better and more correct knowledge! The reason for this critical aftermath, and for the condemnation of a standpoint which was adopted by the overwhelming majority of physicians and investigators who examined the new method, is such a ponderous one that we consider a discussion of the cardinal points in order even to-day. The reason lies in the fear that a repetition of similar events is not beyond the pale of possibilities even in the future. Such a fear is justified especially because the medical profession, always considering it a point of honor to keep in touch with achievements of a *purely scientific* nature, also shows the excusable tendency of adopting dogmas and theories nurtured in the laboratory as generally applicable and as a basis for its views and actions. The catchword of "scientific physician," of a physician who believes it incumbent upon him at once to make modern achievements his own, has, for this reason, too frequently become a pretense for superficial grasping after the latest

views and ideas, for a certain versatility of opinions; and it is necessary at last to proclaim once more that not he is a scientific physician who early appropriates the precipitate of new formulas and ideas, and who, as it were, mechanically applies with uniform lack of criticism everything that is new simply *because it is new* and modern, but that only he is entitled to lay claim to the designation of scientific physician who *thinks and investigates independently*, who, by long-lasting and careful observation of the *vital conditions of the body in health and in disease*, has also acquired the faculty of measuring new theories with true, lasting, objective standards, and of not mistaking the external appearance of objects for their true nature. A physician who knows the true meaning of cleanliness will have judged all the rigmarole of orthodox antiseptics, which is really past us, as he judges the endeavor to attribute the healing of "well-granulating" wounds or healing in general not to natural conditions, but to the accidental application of an "antiseptic" dusting powder. He will not be misled regarding the possibility of restitution of decomposed or destroyed organic tissue by remedies or curative methods any more than by any schematic method of treatment which considers the "disease" but not the patient, and which, in the same manner, means to obtain a sure result of cure, not only in all cases of the same form of disease (or, to be still more specific, in the variety of this form), but, if possible, in processes which are most heterogeneous, etiologically and clinically. Such illusions or misconceptions of pathological processes and cures of disease are favored, however, when the representatives of science induce the physician, who must have confidence in scientific investigations because he is bound actually to rely upon

them unless his profession is to be a mechanic trade, to believe that experimental investigation in the realm of pathology had analogous substrata as clinical treatment, and that disturbances produced experimentally are identical with pathological manifestations which are the object of clinical activity. Even those conclusions are overstepping the mark that assume the vital conditions of lower organisms in the "diseased" animal body to be fully equivalent to those created by the animal experiment.

The above views are not intended to express an underrating of the experiment or of any other method of scientific investigation; they are merely aimed at limiting the boundary lines within which every method of investigation accomplishes corresponding results. For the majority of biological problems encountered at the bedside are, according to their nature, so difficult to recognize that frequently they can be clearly apprehended or sharply formulated only when approached from all sides. The complicated nature of an apparently simple process is often not manifest, as is well known, until the problem is shaped experimentally. I do not deny, as regards, for instance, the question of protective inoculation, which as yet has really been approached only in the animal experiment, the possibility that protective inoculation may be utilized therapeutically, either prophylactically or curatively (*i. e.*, after the outbreak of the disease, not merely after infection has taken place), altho I do not value this possibility very highly. But I demand that the *results, before they acquire practical value*, should first attain such a degree of reliability that, upon the basis thus created, an experiment in man may be ventured, *with the safe presumption that no harm be done, and with the reasonable hope of a certain, altho moderate, suc-*

cess. I demand, therefore, that, before a practical utilization of experimental results is thought of, *all preliminary questions, to be decided by preliminary scientific investigation, be decided unobjectionably*—and such preliminary questions exist in large numbers. The most important one regarding the method of Koch—which, according to our opinion, as repeatedly expressed, should have been decided before the introduction of the method could be thought of—was the *solving of the problem* whether the bacterial product employed by Koch *in reality possessed the specific effect attributed to it by Koch*; whether *only tuberculin*, and not also *other* bacterial products, were capable of producing the same (irritating) effect. It was unquestionably necessary that this preliminary question should have been answered in the affirmative before tuberculin could be recommended as a valuable diagnostic remedy; for, if *other* bacterial products also effect similar manifestations of reaction in the tuberculous, if Koch's preparation produced a reaction also in the *healthy*, or at least in those that were not affected by *tuberculosis* (if this reaction, according to the opinion of Koch, were to be an *absolute requisite of the effect, respectively of the possibility of cure*), then proof had been adduced that in the action of tuberculin, as in the action of any foreign substance, we were dealing *only with an uncommonly strong irritation of the organism* into which the substance was injected, and not with an action which is peculiar only to the products of certain species of bacteria upon identical colonies of bacteria in the tissues. Then it would have been demonstrated that the specificity were only an apparent one, that the phenomena were caused not by the *quality* but by the *quantity of the substance exerting irritative effects and contained in every bacterial extract*.

The next preliminary questions were whether certain general phenomena, occurring with sufficient doses also in the healthy, in particular rises of temperature, would take place also upon incorporation of the products of various forms of microbes, and whether the irritation symptoms are not due to the inferior local irritability and capacity for stimulation of the healthy organism, in the form of a *general* reaction (higher temperature of the body), instead of to *local* irritation in already existing inflammatory disturbances of the tissues. For general reaction is, after all, probably only a minimal local reaction in numerous parts of the body, which, however, does not occur under the picture of special, visible, topical inflammation, simply because in the healthy all tissues possess equal, or at least nearly equal, irritability and capacity for stimulation to inflammatory irritation. Now, if irritability is limited, with a definite dose of the irritant which does not reach the climax, no special subjective or objective symptom will indicate the reaction of the body. According to the proportion of the irritation to the size of this climax—*i. e.*, according to the extent of the irritability, a local or general reaction must develop in the individual case, and the general symptoms will prevail if the irritability is a uniform one, so that the irritant exerts a presumably less irritative effect in all areas in which it is in contact with the tissues, whereas predomination of local reaction (which may often also be combined with general symptoms) will be observed in those cases in which special local irritability is bound to produce an especially marked change of tissue activity even upon the action of an irritation which surpasses the (normal) climax not at all or only very slightly.

Recommendation of the remedy for therapeutic purposes or for the application in man should not have been attempted until after these preliminary investigations had led to an unobjectionable, positive result; until a specific homologous effect had been ascertained and shown that the products of the tubercle bacilli were active in the manner assumed by Koch only in individuals already infected by tuberculosis. Then only was it permissible to think of a specific diagnostic or therapeutic efficacy by way of protective inoculation and not merely of an irritating action of a strong irritant always leading to more or less marked defensive efforts in the organism which are designated—if they last for some time—as pathological symptoms.

It is necessary, finally, in all cases in which it is intended to employ bacterial products for protective inoculation, to examine carefully whether the *method* in use for obtaining the substances in question does not cause the most *efficacious* constituents of the culture, respectively those that best serve the purpose of protective inoculation, to be *destroyed* or *eliminated*; for it can not be denied that, in the treatment of culture media containing the efficacious substances by agents coagulating albumin or by heat at boiling point, just those albuminate combinations are destroyed which, in our opinion, are the most possessed of the power and properties of a vaccine in the stricter sense. We believe that the chemical substances (proteins) remaining *after heating* or *in precipitation* with certain substances will more markedly manifest the action of generators of inflammation than the protective effect of "lymph"—to emphasize with this term at once the character of that substance which is in use in inoculation: *κατ' ἐξοχήν*. We are convinced,

further, that the *protective character of the bacterial products in the widest sense will be the more pronounced* the more its component parts are analogous to those of the "untreated" albumin molecule of the animal blood serum. The more markedly changed—with otherwise equal composition of the molecules—the intramolecular and intermolecular conditions of affinity, the more the bacterial product loses the character as a "vital"¹ substance by definite, interfering methods of treatment, the less will it possess the qualities to which the living cell owes its specific peculiarities in the struggle for existence, and the less will it be suited to put the living cells, as a specific (normal) irritation, into a condition of *accommodation—of non-irritability to foreign, inadequate irritants, which is identical with an inferior display of internal, bodily labor.*

If the above explanations are pursued in all the consequences not especially enlarged upon here, it will be conceivable why the battle of opinions should begin so passionately just on account of the method of Koch. Not merely any new healing method—a daily occurrence—was the object of the contention in this instance, but a new principle of possibly enormous range; the point in question was an idea, the further development of which promised uncommon results for the entire domain of therapy. Besides, this new form of therapy was to stand its test upon a field apparently easy of control, in a form of disease in which undoubtedly the most exact methods of examination at the disposal of medicine could be brought to bear. It appeared easy, therefore, just here to adduce the proof for the correctness of the views from which the new method had grown, and to illustrate

¹ Compare my remarks on "The Living Molecule," in "Grundlagen, Aufgaben und Grenzen der Therapie," p. 138, etc.

in a special case of infectious disease, in tuberculosis, the range of the general law according to which a *remedy was to be sought and to be found in an equal manner for all infectious diseases in protection by inoculation*. But the *trial in man has strikingly shown the complicated conditions existing in the diseased body, the differences presented by the process of development of "disease" as opposed to the sudden occurrence of experimental intoxication or invasion, and it has elucidated even to the skeptic the multiplicity of the problems which render the realm of protective inoculation one most difficult to explore. Therefore, the inconsistencies in the first results of the investigations of Koch's method were due not to the deficiency of observation, and to the partiality of the observers alone, but to the lack of plainness of the view-points which were dominant in the question of protective inoculation, and which permitted not only one of the most difficult problems to appear as disproportionately simple, but also the most unlikely event as absolutely plausible and at the same time answering the purpose. The struggle which was fought and which will be fought for some time to come, was, only with new scenery, the old battle between clinic and laboratory, for the experimenter in biological sciences usually considers biological problems much simpler than the physician who encounters them daily in all their difficulty and variety of form, and he does not, as a rule, reckon with factors, such as predisposition and individuality, which are of greatest importance to the physician, who deals with individuals or with smaller groups of homogeneous individuals and symptoms. The experimenter in the domain of infectious diseases cuts, as it were, the Gordian knot in his experiments, in which from the very onset the effect of individuality is eliminated, in that he poisons all ani-*

mals in the same manner with large quantities of the same irritant (microbes, toxins, etc.), but he does not cause them to *fall sick*, thus creating very *simple conditions, which, however, are not natural and entirely different from those that are in reality observed by the physician*. Of one hundred animals of the same species that he infects, the *whole number falls sick at once*, and it may be expected almost to a certainty that *all these animals, without difference, will die or get well within about the same time*, whereas, of the same number of human beings exposed to a noxa in the usual manner of infection, only a *minority falls sick (the symptoms of the affection in the individual cases will be very varying)*, and a still smaller number, again under *different symptoms of the disease, succumbs at various intervals of time*. Besides, just the opinion of Koch that the point in question in the action of tuberculin was a specific, homologous reaction—an opinion which grew from an insufficient preliminary investigation of the most important points—has immeasurably increased the difficulty of the questions to be decided at the bedside. It is not astonishing, therefore, in view of the complicated questions involved which heretofore had been considered much simpler, that the former standard of judgment failed entirely in many clinicians and physicians.

The history of the Koch method has clearly demonstrated the sources of error included in the apparently simple experiment—sources which are the greater, the simpler the experiment appeared at the beginning. We should from this learn the lesson: *not to make further investigations concerning PROTECTIVE INOCULATION the starting-point for the practise of medicine until all view-points—and they are not all even formulated as yet—have found*

due consideration in the preliminary investigations. The results can not be utilized with certainty until it is thoroughly understood that INJECTION DISEASE and *infection* disease are qualitatively different, in no form to be compared, since PREDISPOSITION can not come to its own in the former case. But, moreover—and this is a very important point—it is not the purpose of the *therapy of "disease,"* as in the attempt at curing the results of an infection created experimentally, to prevent certain quantities of bacteria *solely and exclusively from colonizing in the tissues*—immediately after the injection they do not yet adhere to the tissues, and a goodly part of the phenomena taking place at the beginning (including, probably, rapidly occurring death) is the effect of the simultaneously injected toxins—but *to render harmless the colonies already developed, which have long since adapted themselves to the vital conditions of their host and have escaped his eliminative powers by tissue changes.* But the possibility is a *very limited one* that the remedy employed *also reaches these colonies which, after they have stayed in the body for some time, are always situated within the tissue changes.* This is the quintessence of the whole question.

Protective inoculation, therefore, may have a certain future, but before success is assured it must be shown, first, that it also serves *curative*, and not, as in the present form of inoculation, merely *prophylactic* purposes; secondly, what *quantity of the inoculation material displays the maximum of curative action with the minimum of other irritative effects;* thirdly, whether some *other mode* of developing the bacterial products than that customary so far should not be employed to *preserve* the constituents with which the *protective power* is combined, and to *isolate them completely from the other indifferent or even harmful com-*

ponents. As yet it is not demonstrated that the *proteins* are capable of thorough immunization, but it is proved that toxalbumins possess this action. This is indicated not only by the experiment, but, to a certain extent, also by typical vaccination. But it is probable that the bacterial product which is to offer protection by inoculation must not be developed or mitigated upon artificial media, but through intervention of an intermediate host—of a living organism. This question has become further complicated, in that lately attention has been drawn to another form of immunization—namely, that which is effected by so-called ANTITOXIN. To allude briefly to this subject it is assumed—altho, according to our opinion, not on the basis of stringent statements and observations—that an infected animal develops in the course of the infection so-called antitoxin—*i.e.*, substances which possibly cause immunization of the infected animal or prevent the progress of the affection. It is believed, further, that such substances, taken from the poisoned animal and injected into other animals, will produce immunity in the latter even *some time after infection has taken place.* These antitoxins, dissolved in serum, are said, according to some authors, to develop from the toxin under febrile manifestations. To form antitoxin without the intervention of foreign blood has not been accomplished up to date. The question of antitoxins is as yet not ready for decision in any direction, for it is neither probable that *antitoxin* is developed from *toxin*, nor that *antitoxin* is a *specific* substance different in every instance, according to the species of the generator of the infection. Much more probable is the view that the capacity for immunization is a general quality of the living molecule in the serum, and that the

serum acts as an irritant which, in a foreign organism, produces that adaptation which accords protection from greater irritants—*i.e.*, renders the inoculated organism void of reaction to the introduction of similar irritants not surpassing a certain degree. This lack of reaction prevents the foreign body producing increased transpositions in the body (increase of the entire internal work of the body); it does not permit the occurrence of that profuse saturation of the (abnormally) irritated tissues with nutritive material from which the foreign irritant, the microbe, obtains, at the expense of its host, the amounts of energy necessary to its existence and to its propagation—both qualities of the microbes are really correlates—and thus it brings about, finally, that the *foreign agent, without having exercised any special influence upon the internal (essential) labor of the body, leaves the body without causing evil effects, by the usual form of excretion* (by way of increase of the *extra-bodily* labor). Therefore, at the onset of infection, the difference between the conduct of the inoculated, immune (void of reaction) organism and the non-inoculated one which responds to a certain irritation with an increase of the internal activity of the tissues, consists, above all, in the fact that, in the former case, it falls to the share of the organism—apart from the irritation exerted by the toxins still contained in the bodies of the bacteria—that it must only mechanically eliminate a foreign body or foreign agent of *very small dimensions*, whereas, in the latter case, the internal activity (processes of oxidation in the tissues, the production of leucocytes, the endo-cellular processes) assumes a constantly increasing range, all the more extensive the more the production of the abnormal irritation is increased in ever rising propor-

tions, under these conditions favoring the development of the noxa (if this be a microbe). In the former case, therefore, we are dealing with *purely mechanical effects*, at most with benign smallest emboli, an increase of the excretory activity of the kidneys, similar as in the excretion of smallest crystals of uric acid, of smallest corpuscular constituents, destroyed microbes, etc.; the second case presents, besides the manifestations of *local inflammation*, more or less *marked general phenomena* which form the summation of the different items of locally increased tissue activity. The amounts of energy produced in inflammation by the maximal irritation are not employed in a physiological manner for the performance of *external* (EXTRA-BODILY) labor, but for the performance of *increased ESSENTIAL, internal, labor*. A muscle, for instance, which responds to the ordinary irritation with *contraction* and to an increase of the physiological irritation with *tonic contraction* (greatest physiological performance, greatest increase of the extra-bodily labor)—a muscle that consumes only a small portion of the energies for essential (internal) labor, for the causation of the altered combination of molecules and atoms in the tissues which create the physico-chemical fundamental conditions for the possibility of contraction, *does by no means respond to the (pathological) irritation surpassing the extent of the physiological action of the irritation, directly with an increase of the extra-bodily labor, but it augments its essential (internal) labor, in that it produces, above all, heat*. Whereas, therefore, extra-bodily activity, serving physiological purposes, promotes the *purposes of the organism*, ingestion of food, defense against external influences, adaptation to foreign influences;

whereas, under physiological conditions, the *irritative quantity created continually anew by the organism in the activity serving the purpose of its preservation, is the regulator of labor in general*; another form of labor will be the determining factor in case there becomes active in the organism an irritation (microbes, etc.) which has not developed autochthonously, answering the prevailing demands and performances, but which is really foreign to the purposes of the organism. Then *internal tissue activity becomes increased—i.e., that form of activity which does not serve directly to the mediation of the relations of the body to the external world, but which supplies the energy which guarantees the cohesion of the various elementary constituents of the tissue, the preservation of the smallest protoplasm machine, of the ENERGETE according to our designation, and the combination of the various small organic machines into the complex forming the functional labor unit, the individual.* This aggregate of essential (internal) labor is required to furnish to a certain aggregate of protoplasm, to a complex of functionally different, smallest organic machines, the functional unit and, with it, the faculty of performing extra-bodily labor and, by appropriate alteration of the sum of this labor, according to all alterations of the outer world, again acquire the energy required for the performance of essential (internal) labor. This auto-regulation of the organic machine depends upon the biological fundamental law; it is the expression of the law of the preservation of energy to which also the performance of the protoplasm machine is subject in the conditions of normal and pathological labor. The fundamental condition is the presence of the molecules which supply the mechanical basis for the special form of auto-

regulation, for the production and preservation of processes of causation, and which again are derived from living molecules. To disease as well as to health applies the postulate. The greater the irritation for the essential (internal) labor and the greater the corresponding irritability (*i.e.*, the amount of labor required for the mere preservation of the machine), the less extra-bodily performance will be possible. *An increase of the essential (internal) labor can be accomplished only at the expense of the extra bodily performance.* Every irritation capable of increasing essential (internal) labor, owing to a certain form of irritability of the tissue, is the more pernicious to the organism the more continuously it operates. Microbes are the strongest irritants for essential (internal) labor; hence, the cause of a display of energy which, in a measure, is unnecessary for the real purposes of the organism. The organism must perform increased labor to support the foreign organisms that produce irritation, and which it can not eliminate with the aid of the processes of oxidation or by simple mechanical excretion. Then microbes are parasites in the true sense of the word. . . .

Thus it is probably definitely shown that the primary method of Koch has not stood the test, and it is further likely—unless new *exact experiments should show an immunizing action of most minimal quantities of these substances—that BACTERIAL PROTEINS do not exert any protective effect worth mentioning, and, therefore, will not prove useful for therapeutic purposes.* The reason for this, as we wish to emphasize once more, is due to the fact that a bacterial protein as a substance producing irritation is probably never capable of causing that condition of *non-irritability which constitutes the sign of successful protection*

by inoculation in the already *functionally irritated* areas not yet affected by the bacterial invasion or adjacent to the focus of the disease, which should be the principal object of immunization. The point in question is not merely to cause the action of a very extensive irritation at any price, and to produce a *reaction*, but to render the inoculated organism *void of reaction* to certain irritations of carriers of infection—an essential part of the effect of protection by inoculation. This alone would mean to effect IMMUNIZATION. Immunization is a sort of functional adaptation; therefore, it can be effected only by minimal irritation which, analogous to the processes in exercise, exerts a modified influence on the causation of essential (internal) labor, and diminishes that for the causation of EXTRA-BODILY labor, in that, by the production of minimal changes of the *physical* properties of the tissue, it prevents a similar (and even a stronger) foreign irritant (for instance, the living molecules of the microbes) from effecting an increase of the ESSENTIAL (INTERNAL) LABOR—*i.e.*, from a more potent display of energy for the powers that guarantee the cohesion of the tissues and for the synergy of the parts. But the above-mentioned reduction of the irritability to essential (*foreign*) irritations formed by the organism, or the diminution of the normal demands of the tissue regarding the performance of essential (internal) labor, is even compatible with an *increase of the functional capacity* as related to extra-bodily labor; for the reflex (excretory) activity of an organ may even be increased in spite of the apparently lowered *irritability*. The kidney, for instance, may perform an increased (external) labor without being inflamed, as is the case

in REGULATORY ALBUMINURIA (Rosenbach), in hemoglobinuria. Just because the free, non-usable albumin or hemoglobin does not constitute a stimulation of the kidney to *essential (internal)* labor, the organ is capable of excreting considerable quantities of these substances without disturbance of the internal activity of the tissues, without increase of the essential labor in the secreting tissue—*i.e.*, without inflammation—and to rid the body of foreign, harmful constituents just by virtue of their extra-bodily activity. In other cases, on the contrary, in which these substances which are heterogeneous, or have become foreign, to the organism, act as irritation to essential labor because the irritability of the organ permits it (because the organ has not attained the required adaptation), there takes place an inflammation of the kidney—*i.e.*, the condition of increased internal labor which is always associated with diminution of extra-bodily capacity of function, with decrease of urinary secretion and excretion. An irritant, therefore, which is introduced into the body to produce a healing effect, must, under no circumstances, act locally or upon the entire organism with those qualities which characterize the *inflammatory*—hence, acutely stimulating—*irritant*. *An irritant which is to cause adaptation must not go beyond the limits of mild functional irritations (of the processes of causation which regulate the functions of the body)*. An adaptation due to this irritant is analogous to that process which we designate practise—*i.e.*, mild functional irritants which increase extra-bodily activity without *augmenting essential (internal) labor*, heighten the function, render the organism more capable of action, whereas *inflammatory irritants, to the action of which the body must respond with the transformation of great*

quantities of energy, require a waste of energy, in that they increase the internal (essential) labor at the expense of function, of the extra-bodily activity. In other words, an irritant with inflammatory effects which acts upon an organ—for instance, the kidney—does not cause an increase of the real excretory function of the kidney, but it changes the *form of renal activity* entirely; it heightens the transformation of the amounts of energy and the production of living force, but the labor thus produced is consumed in the tissue itself. Lively changes in the tissues take place, accompanied with a rise of temperature, but all these transpositions and transformations of the energy on hand do not increase what we denominate performance for the purposes of the organism. Since labor is performed only by the transformation of the energy on hand, the increase of essential labor necessitated by the inflammatory irritation is bound to decrease the real *extra-bodily* labor of the machine—*i. e.*, the externally visible performance of labor (for instance, in the kidney, the mechanical elimination of the non-usable substances)—by the same amount by which the internal activity is increased of the different tissue constituents, the smallest protoplasm machines, and the large mechanism, the functional unit, accomplishes less because the consumption of energy has been increased for the separately working components. The larger quantity of blood in the organs, the abundant formation and accumulation of leucocytes, etc., represent the essential labor performed by the tissue which, under such circumstances, naturally becomes all the less suitable for the other functions to be performed by the multitude of smallest tissue components constituting the unit of the machine, the greater the sum of internal labor to be per-

formed. To immunize, therefore, we must not look for irritants which produce active, inflammatory (febrile) reaction (increase of essential labor which leads, at first, to transitory, later, to permanent, changes of tissue), but we should select substances which act *only by increase of function—i.e.*, which, equal to the adequate irritants of normal metabolism, increase only extra-bodily labor, the mechanical performance of labor for the purposes of the organism; for this form of labor, which guarantees nutrition, preservation, and the uninterrupted performance of the functions of the body, is promoted solely by the manifestation of function—by auto-regulation, as it were. But an organ is strengthened, and thus becomes more capable of function, by performances of a purely functional character, which are interrupted by appropriate intervals of rest for the preservation of energy, *i.e.*, the accumulation and development of new energy—whereas it suffers a more or less considerable disturbance of function by exciting, inflammatory irritations which necessitate an acute exertion of numerous manifestations of energy in the tissue itself, and which lay claim to a great portion or even the entire amount of energy available for extra-bodily labor. In fact, even the mechanism itself, the substratum of the apparatus in which the processes take place, becomes affected. If, as we believe, immunization is adaptation, then an irritant must be found corresponding in quantity and quality to the normal functional one, which, as in the process of practise, by gradual habitation to the weaker disturbance, enables the tissues to react to stronger irritants with *increased function* (extra-bodily activity, mechanical labor, muscular activity, elimination, increased faculty of excretion), but not with *increase of irritability, ultimately leading to*

an alteration of internal labor which we call inflammatory change of tissue. Decrease of irritability, hence adaptation with unchanged capacity of function for extra-bodily labor, is the purpose of protective inoculation, and this end can probably be attained best by smallest quantities of those small complicated albuminous bodies which we call TOXALBUMINS and which are closely related to the substances already contained in the serum. These albuminous bodies of the blood are, as is well known, the carriers and representatives of the exciting powers which we designate as the normal irritants for the activity of the organism. The question as to the composition of these bodies, their origin and the experimental examination of their action upon foreign organisms is the most burning question of medical science. Upon its solution depends the future of scientific therapy, which is to be determined, and hence to be promoted, in the laboratory—at least, in respect to all its preliminary experiments. It appears as if upon the solution of this question depends essential reform not only in all therapeutico-medical views, but also in the fundamental biological views, the expression of which are the prevailing therapeutic standpoints. However, according to our opinion, the chances for real therapeutic success in this direction are as yet very small indeed, and we believe that the roads of experimental therapeutic investigation will for some time to come again run in a direction different from those of clinical research, and for the present we may say of the union between experimental science and the clinic as of the association of philosophy with natural science: “Enmity be between you, alliance is premature!” One more point may be emphasized to illustrate the difficulty of the question of the importance of the curative serum and of the antitoxins: *There is little*

probability that we are here dealing with chemically characterized bodies of definite composition ; what characterizes the immunizing substance, respectively that one which acts as curative agent, is the sum total of living force with which it is endowed. The combination and the motility of the atoms are the characteristics of the agents in question, not their composition regarding the number or mutual grouping of the atoms in the molecule. They must be "living molecules," molecules equipped with a certain amount of free living force, and by this differentiated from equally constituted, indifferent, dead molecules. But since all our methods for obtaining substances from living organisms furnish only dead molecules, in which living forces (strongest vibrations) are no longer present, serviceable inoculation material which must contain "living molecules" can be taken only through the intervention of a living intermediate carrier from whom inoculation material is taken. And this inoculation substratum must contain a still more active form of the molecular powers than in the "indifferent" serum, for only from animals already immunized can the irritant be taken calling forth the condition of adaptation and non-irritability, which is the characteristic of immunity. Active molecules, therefore, must be capable of transmitting to the molecules of the inoculated organism a form of motion analogous to their own main quality. Certain analogies to the processes interesting us here are offered in the domain of physics by the phenomena of magnetism, polarization of light, etc.

If, therefore, we trace the efficacy of a vaccine in its widest sense to *more active*, intramolecular and intermolecular, motion of certain albuminous bodies contained in it, it is obvious that, according to our opinion, this

immunizing power can become manifest only upon *direct incorporation* of the material in question into the *blood* (by subcutaneous application), since the "living" albumin forming the most essential constituent is altered in any other method of incorporation, and is transformed into "ineffective" dead material. The action of the gastric juice, for instance, is bound, owing to the coagulation of the albuminates, to neutralize any immunizing effect, and hence we doubt *a priori* the demonstrative power of experiments in which immunity of nurslings is said to be brought about by the ingestion per os of milk from immune wet-nurses. Efficacious from the stomach and also from the intestine are only substances the active principle of which is not combined with the "living" albumin; thus, even tuberculin introduced per os or per rectum is absolutely without effect.

With due reserve, we also wish to express the supposition that the infecting agent of *constitutional syphilis* is not a microbe, but, above all, some form of vaccine which owes its effects to "living" albumin molecules.

XV

THE COMMA BACILLUS, MEDICAL SCIENCE, AND THE MEDICAL PROFESSION

ALTHO in the following paragraphs I intend merely to call attention to the great harm that has been done and will be done to the medical profession, I can not forbear touching with a few words upon the scientific aspect of the question. For I believe the undeniable harm done to the authority of the physician, the nonsensical cholera-phobia of the public, and the indifference with which, in consequence of this fear, the most deplorable encroachments upon the personal liberty of the individual have been considered as matters of course, are the unavoidable results of the modern theory of infection or, to use the popular term, of the bacillary theory.

Has the course of the epidemic in Europe, and especially in Germany, proved that the comma bacilli are the cause of the origin of the malady; has the course of the epidemic up to the present furnished even the shadow of an unobjectionable proof that the modern theory has solved the problem of the origin of this pestilence? No need to quote Stanhope¹ to demonstrate the non-contagiousness of cholera, for no one will seriously believe that he obtained his immunity through inoculation, as nurses and physicians have furnished a much more convincing

¹ An English reporter who, after previous protective inoculation, came in close contact with cholera patients without becoming affected.

proof, and as, in spite of the alleged infection of our rivers and in spite of the many sailors afflicted with diarrhea and comma bacilli, the disease fortunately attained but a small foothold outside of Hamburg. Had Stanhope become affected, he would have proved to a certainty that his protective inoculation was an illusion; but that would not have furnished any proof that cholera is infectious, and that the bacillus is the carrier of the infection. For this proof can only be adduced in a locality heretofore *immune to cholera*, and in that some one falls ill from eating cholera bacilli, or in consequence of nursing an individual who had been infected *at some other place*. Even then the proof would not be absolute until the immunity of the locality is shown to be actual, in that *no further cases of cholera* occur in this locality after the first patient had been isolated. If, in case these experiments remained without result, in order to solve the theory of the etiological importance of the comma bacillus, objection should be made that the person experimented upon, owing to healthy *digestive* organs, did not furnish a suitable soil for the bacillus, and if logically it should be demanded that before entering upon such an experiment the stomach be sterilized, and that peristalsis be arrested by opium, such demands could clearly demonstrate how far, in our inclination to experimental pathology, we have strayed from the true conception of the character of the "affection."

If only such a considerable functional insufficiency of the digestive apparatus must be the preliminary condition of infection by a micro-organism, then the microbe is most unessential, and *it must be explained, above all, why such a large number of persons, just at a stated period, become affected by such a weakness of the digestive appa-*

ratus. It requires an explanation why these weak individuals *do not also fall a prey to other bacilli*. Or is it claimed that these, too, succumb to the dominating influence of the comma bacillus? This can scarcely be the case, since the contents of the intestines always show other microbes besides the comma bacillus. The cholera patients do not die because they fall a prey to the bacilli, but they die because of the *most acute functional insufficiency of the intestinal tract*, which favors not only the multiplication of comma bacilli, but that of any other species of intestinal parasites. It appears only that in many cases, but by no means in every instance, the comma bacilli or spirilli are more readily cultured on artificial media than other forms.

And what arbitrary methods in diagnosis did this yearning after the demonstration of the comma bacillus bring forth! I surely do not occupy the standpoint that it is the first duty of the physician to make a schematic school diagnosis at any price; but if a diagnosis is to be made in the usual manner, if a series of essential changes of function must be present to classify the picture of the affection—*i.e.*, to designate it by a proper name—we can and must demand, above all, that the diagnosis be not formulated from a so-called pathognomonic symptom, and *that quite arbitrarily from a series of signs one sign be not pushed forward as the one and only essential for the ultimate definition*. The presence of tubercle bacilli in the sputum suffices by no means to diagnosticate what, clinically, we call pulmonary tuberculosis, for, quite apart from the fact that the bacilli may in some cases have accidentally entered the lungs in the same manner as dust or other foreign bodies, the demonstration of tubercle bacilli neither proves that absolute proc-

esses of destruction are present in the lungs, nor that the process is incurable, and hence must be progressive. We only know empirically that, in localities in which bacilli are found, a definite predisposition to decay of the pulmonary tissue is present, just as we know empirically that such is the case in individuals with hereditary or congenital disposition—*i. e.*, children with narrow, long thorax, have a tendency to affections of the lungs in which tubercle bacilli and other forms, especially pyococci, develop in large numbers. *Diagnosis and prognosis, therefore, can not be deduced from the sputum*, but only from the results furnished by a careful examination of the whole diseased organism, and we actually find that individuals with numerous bacilli are frequently in better health and present better chances for recovery than those whose sputum shows only a few bacilli. Any one who wishes to speak of phthisis bacillaria can not be denied this privilege; he then creates a special picture of disease or, more correctly, a conception of disease which, however, does not specify anything of importance to the physician or to the patient, and it can not be maintained that anything has been gained by this new designation. Only a new *principle of classification* has been created which, however, ranges *curable* and *incurable* cases in a uniform manner in the same category. Thus there can be no doubt that comma bacilli can frequently be cultivated from severe cases of *epidemic intestinal insufficiency*; but to make the presence of comma bacilli a principle of classification collides with the demands of logic, since cases which show comma bacilli and those in which these bacilli are not present are not *principally different*, neither with reference to the organic disease at the bottom of the pathological picture, nor in regard to the out-

come. The fact that *comma bacilli* may be cultivated from the intestine announces neither the severity of the case nor its epidemiological significance, for individuals who have bacilli and those that have not die at the same periods and under the same conditions under the clinical picture of cholera (of the most acute insufficiency of the intestine). How is it possible, therefore, that the case differs principally from the other, in that bacilli are found in the one instance and none is present in the other? Other individuals, again, show *numerous bacilli* and do not present any threatening phenomena (at most, a watery discharge), and they recover in a short time, in spite of their dejections containing comma bacilli; whereas others, from whose discharges the bacilli can be cultivated only with the greatest difficulty and after several days' trials, have long been dead when this proof is furnished. Hence, how is it possible that *the bacilli are the cause of the manifestations when cause and effect are in such a marked contrast?* If a primary weakness of the digestive organs furnished the predisposition to the colonization of the bacilli, it would at least be fair to assume that *the greatest number of bacilli were also the expression of the greatest weakness of the digestive organs.* But nothing of the kind is the case, and still the bacilli are credited with being the cause of the epidemic, whereas the great number of the other factors acting upon the body, which create the fatal insufficiency of the intestine, are not considered. How else, from the standpoint of the bacillary theory, can the fact be explained that every year in the summer months *insufficiency of the intestine of nurslings and smallest children becomes epidemic only in the so-called lowest classes?* No infection and no bacillus can be demonstrated in this case;

only the fact remains *that the children of the poorest part of the population succumb in greatest numbers to an epidemic.*

Neither the theory of the ground-water nor the theory of the comma bacillus furnish an explanation for the origin of the epidemic occurrence of the intestinal phenomena constituting the picture of cholera and that of cholera morbus. The bacillus is surely an accident, no essential cause in a logical sense. The condition of the ground-water, however, may announce that one of the factors that influence the activity of the body in general and, with it, that of the intestine (in a manner not determined as yet), has materially changed. But a certain condition of the ground-water is surely only a secondary phenomenon—a phenomenon that is synchronous with cholera, but not in a causal relation with the same.¹ As little as the advent of the birds of passage is really spring—altho the appearance of spring is in a certain time relation to the advent of the birds—just so little is one of the causes so far given the real and sole cause of the occurrence of that pandemic and epidemic insufficiency of the intestine of adults which we call cholera. What explanation has been furnished by the theory of the comma bacillus regarding the propagation of the pestilence? Since the bacilli do not travel up stream they must be carried by human beings, and great pains are taken to demonstrate this method of infection everywhere, altho even now plenty of instances are at hand in which a connection with introduction can not be determined. If, in spite of the assumed infection of all the

¹ von Pettenkofer, in his excellent criticism of the report of the German Cholera Commission (Munich, 1888)—more worth reading to-day than ever—says: "Its variation (that of the ground-water) is under some circumstances only a good indication of processes in the layers of soil above it."

rivers, so few cases of the affection have occurred even among fishermen and sailors, either infection can not be in evidence, after all, or, if this be the case, it can not be as dangerous as assumed at present. And since there can scarcely be any question that the crews of vessels, to whom now the rôle of transmitter is preferably attributed, were at the beginning only to a very small part subjected to any control or could at all be controlled, it is very probable that by far more carriers of the toxin (in the sense of those who assume this method of transmission) have slipped through than were subjected to measures for protection. Necessarily so many more must have escaped these measures as also the apparently healthy may harbor large numbers of comma bacilli. Nothing shows more plainly than this comparatively marked immunity even of sailors how insecure is the theory of transportation of the toxin of cholera and the theory of infection from man to man. So long as the conditions for the development of intestinal insufficiency are absent, so long is even the comma bacillus powerless, and even the proof of its presence in a river, if furnished unobjectionably, would not, in our opinion, justify the unquestionable conclusion of the water being infected, quite as little as the finding in any body of water of bacilli of the typhoid variety, admits of the conclusion that this water is the cause of an epidemic of typhoid, for, singularly enough, the cultures of all these bacilli always lack some, altho allegedly unessential, characteristics of those which are cultivated directly from human tissues. It is our opinion that microbes also show essential variations in their behavior, according to the soil upon which they have grown, and according to the developmental conditions upon which they depend. Here,

too, convincing demonstration is wanting that the bacilli really have only *constant* characteristics, and that, in common with every living organism under varying external conditions to which the bacilli also must adapt themselves, thus *undergo a change of qualities which we are only erroneously inclined to regard as essential.*¹ Thus

¹ We desire to quote a small table taken from an article written at our instigation by J. Rosenthal, in "Die Wandlungen in der Lehre vom Kommabacillus Koch's im ersten Jahrzehnt." *Wiener med. Presse*, 1895, No. 42, etc.:

Formerly.

The cholera bacillus is the only comma bacillus.

The characteristic feature is the comma.

Koch's bacillus is merely of the form commonly spoken of as comma.

The number of the worm-screws ranges from 8 to 30.

Puncture culture with "air bubble," the potato culture, the resemblance to glass particles, are of great importance.

Liquefaction of gelatin is a characteristically slow one, as in no other microbes.

Transparency of the images.

Phosphorescence of the pure cultures does not exist in the true cholera vibrio.

Microscopy is of lesser value as against culture.

Cholera bacilli flourish best in a temperature of 30°-40° C. (86°-104° F.).

Cholera bacilli are aerobic.

Artificial infection of an animal body is impossible.

Now.

Comma bacilli are known to us by the dozens of species.

The characteristic feature is the formation of spirilli and undulating motion.

Koch's bacillus, in contrast to others, is characterized by uniform thickness and curvature.

According to others (Finkler 3 to 6, Deneke, 4 to 20) eventually the same number.

No longer of any importance whatever.

Other bacilli may also, if properly treated, liquefy gelatin slowly.

Other bacteria also manifest these to a certain degree.

Phosphorescence appears to be demonstrated.

Microscopy prevails over culture ("cast of net").

Cholera bacilli require *exactly* 22° C. (71.6-11.0° F.); otherwise unavoidably confused with others (Finkler).

Cholera bacilli are capable of facultative anaerobiosis.

The animal experiment is not only positive, but it is also an *important* link in the chain of diagnostic signs.

the question is not decided yet whether or not the bacillus of abdominal typhus and the bacterium coli commune are closely related, and whether or not the latter is or becomes pathogenic only in a distinct predisposition of the host. Many cases from every-day practise which remain isolated, while no other typhoid patient can be found in the entire locality, point to the latter assumption.

If water were the carrier of all these infections, if it were so easy to infect rivers that no method of filtration would any longer afford protection, and that boiling alone would be of avail (which might possibly furnish a drink not conducive to digestion), the question arises: For what purpose do we build water-works at great cost which obtain their supply of water from rivers? For, if we are permitted to drink boiled water only, we might, with advantage to ourselves, return to the former system of water-supply from wells. Or should these directions and precautionary measures hold good only in times of an epidemic? Such can not possibly be the case, since, according to the opinion of the adherents of the prevailing infection theory, *one* case suffices to infect the water and serve as focus of dissemination. Hence, care should be had at all times, and from now on only boiled water must be utilized. Unfortunately, in spite of this apparently safe conclusion, the problem remains for practical purposes why epidemics occur so rarely, altho, with modern conditions of transportation and travel, transmission should really take place continuously. A later period may possibly recognize *that the causes of many epidemics should not be looked for in a contagium vivum or in a toxic substance contained in the water, but in other factors which, possibly in connection*

with a certain condition of the water, so monopolize and impair the functions of the organism that many individuals succumb to the increased demands. A later period may possibly furnish the proof, unobjectionable also for those that at present are prejudiced, that man is by no means the carrier of the cholera toxin, and that cholera is not disseminated by toxin and infection, any more than the premature falling of the leaves from the trees is a sign of contagion or infection of the trees. When this knowledge will have general prevalence, those unfortunate enough to live in a period of pestilence will be spared from the deplorable spectacle of having the terrors of an epidemic boundlessly enhanced by the dread of the neighbor, the carrier of the toxin.

However, besides these deplorably inhumane disturbances of the social organism, the foundation of which should be formed by the law of neighborly love, modern science of infection has exerted an influence, especially pernicious, as I believe, upon the *social condition of practising physicians*, in that it transfers the *center of medical production into the laboratory*. This trend of events harbors a pitiful irony. In the striving for most exact knowledge of the processes in the diseased body, methods and auxiliary methods were invented to penetrate into the interior of these disturbances of function and of tissue until finally the pursuit of these aims has gone so far that *the object, the diseased organism, has been lost sight of over the method*. Development of the most subtle specialties has caused the belief to be *awakened that the most refined diagnosis were to have in its train also the best therapy, and we have finally attained a point at which artificial diagnosis is regarded as self-sufficient aim*. The patient was a "beautiful case," and his lesser

and greater sufferings had become insignificant against the great satisfaction of the possibility of an "exact" diagnosis. And since diagnosis no longer had an eye for the functional disturbances, but searched for a pathognomonic, specific symptom, an arbitrarily chosen, mostly unessential symptom which, as in every artificial system of classification, renders immediate determination feasible even to the superficial, we have witnessed that the *diagnosis in absentia* came into fashion, in that any chemical laboratory could diagnosticate from the urine alone the anomalies of sugar and albumin excretions (yes, even certain organic affections), and could determine prognosis and therapy from the percentages in the urine of sugar and albumin. Thus we have seen that the pathologist determined from the microscopical preparation whether a tumor was benign or malign, so that diagnosis, prognosis, and therapy were dependent, as it were, upon his decision, altho he had seen only tumor particles but no patient. The proper foundation and justification were furnished for all these aberrations of the views as to the aims and methods of medical activity by the one-sided development of bacteriological technics. For now *diagnosis, prognosis, and therapy* were supplied *in the simplest manner imaginable*, and the patient, after he had furnished his secretion or excretion, was really superfluous in the subsequent proceedings. The microbe was determined, its mode of living investigated in the test-tube, and the means which, under these, unquestionably fully homogeneous (?) conditions of life, prevented its development, were naturally, with logical sequence, also the most important therapeutic agents, whereas those substances or factors which promoted its growth were by the same token the enemies of recovery.

If a bacillus is destroyed in so and so many pro mille of corrosive sublimate, then it is only necessary to administer to the patient such a dose of this "effective and harmless substance" as was exactly determined in the test-tube, and he would as surely be delivered of his enemies as he would surely be their prey if he partakes of a substance in which they might possibly develop. Hence, butter and cheese must be strictly avoided in cholera times.

Unfortunately, this beautiful idea of being diagnostician, therapist, and pharmacologist at the same time, and of being capable of directing the destiny of man in the most ideal manner far from the paltriness and misery of the sick-bed, too soon turned out to be a dream, and gradually the perception once more begins to ripen that *diseased man*, after all (*even after the axiom in mathematics that the whole is more than each individual part*), not only from the human, but also from the practical, standpoint, owing to the possibility of rendering assistance, *deserved of more consideration than his excretions*. Very helpful to attain this end was the era of tuberculin, which demonstrated to him who was ready to see, with most desirable distinctness, where a science is bound to lead us which considers the patient as an negligible quantity, and, regarding his condition of reaction, places him on the same footing with a dead culture medium.

All experiences of medical art—for the determination of the condition of the organs and their influence upon the general health, in order to fulfil the physician's duty of giving advice and formulating prospects for the future still remains an art, and one most difficult of acquisition—appeared suddenly to be entirely worthless, for the de-

monstration of bacilli did not require a physician, and *their presence or absence furnished both prognosis and therapy*. And since the cooperation of the practitioner was, accordingly, really superfluous, it follows that only physicians of a higher order who were actually qualified to observe—how could an every-day practitioner be capable of such scientific accomplishments?—should be entrusted with the administration of tuberculin; they alone should be permitted to undertake the determining observations of temperature changes, and to attend, according to directions, to the prescribed increase of the doses for the welfare of the sick.

Fortunately, here too the course of events has shown that the destiny of patients must not be decided in the laboratory, and that neither the healthy nor the sick can do without a physician who *decides upon the hygienic measures that serve for the welfare of the sick, and that protect the healthy from disease only after careful consideration of all circumstances, and after most painstaking examination*.

But the power of modern theories and their striving for manifestation in practise has remained the same, and, tho we may predict on the basis of a certain medical experience that the experiments, so very interesting from a scientific standpoint, of inventing new methods of immunization and inoculation *will remain unimportant for utilization in practise, still the claim of bacteriology to control the sole determining vote in diagnosis* will continue to prevail for some time to come, since the perception has not yet become potential that the *diagnostic principle*, which bacteriology endeavors to put forth as the only correct one, *considers neither the requirements of logic nor practical necessity*. For what do we need physicians if the diagnosis of cholera can be made, not from the clinical pic-

ture of the disease, which, unfortunately, permits of so little doubt, but solely in the laboratory, without knowledge of the external conditions, without examination of the patient? *What opinion is the layman to form of the position of the physician and of the importance of the examination of the patient and of the diagnosis, if possibly three to four days may pass before the decision is received from the laboratory whether the patient has succumbed "only" to cholera nostras or—a horrible death—to Asiatic cholera? Must not doubts be aroused whether, in view of the much emphasized difference between both diseases, the physician in charge, who for so long remains in complete ignorance with reference to the nature of the pathological process, might not likewise have made a mistake in treatment? What now distinguishes the graduated physician from the layman? What is the advantage of zealously and diligently studying pathology, of visiting the clinic, if one is unable and dare not make a determining diagnosis? It would then be better to study only bacteriology, and, like a defunct class of wondercure quacks, merely pursue the examination of the "excretions and secretions" far from the bedside. And what, after all, is the result of the methods of examination of the present day? The number of those that have succumbed to cholera nostras (in those districts allegedly not affected by the epidemic) has grown enormously; the disease which heretofore had been looked upon as absolutely harmless for the healthy adult now ranges among those that present the most unfavorable prognosis, whereas, on the other hand, many patients suffering from Asiatic cholera recover, and not a few cases that are distinguished by their wealth of comma bacilli run a milder course than the mildest cases of summer diarrhea.*

One need not be a pessimist to imagine the conse-

quences of the present theory as very harmful to medical science and its medical representatives if it should continue so autocratically to influence hygienic and medical measures; for since *constantly a greater number of forms of maladies is placed in the category of infectious diseases*, diagnosis will gradually be transferred from the bedside to *bacteriological institutions* supported by the state, and from the *medical practitioner to government employees*. Physicians and laymen must get accustomed to the fact that so-called sanitary measures to be taken must be based simply and solely upon *scientifico-bureaucratic principles*, hence not in accordance to the special case, *but in keeping with a scheme*. *With this, naturally, the activity of the physician is at an end, since he is to individualize, and must not make the disease but the patient the subject of his interest and study*. The beautiful and humane calling of the physician to be adviser and helper to man will then have ceased to exist; for consciousness of the *responsibility for the life of the patient is replaced by the fear that a paragraph of a pest law may have been violated, and in place of surety resulting from experience in the treatment of disease there will be uncertainty arising from the fact that the bacteriological diagnosis of a theorist is capable of upsetting all achievements of conscientious medical observations*. Should physicians take no note of these serious considerations concerning the future of the medical profession? Should they not attempt to defend themselves against the surely *threatening danger*? Should not those who see the safety of their profession in the disciplining of physicians rather concentrate their energy and their intelligence upon the defeat of measures which are sure to bring about the most serious harm that has ever befallen the medical profession?

XVI

THE CHOLERA QUESTION

I¹

PROFESSOR DR. ROSENBACH: The discourse just held (by Professor Flügge) was very instructive in more than one direction, for it shows the point to which we are steering if the prevailing scientific theories are still further converted into deeds; and it distinctly points out, further, the inconsistencies between theory and practise. Nothing is calculated to throw a better light upon the difficulties encountered in the establishment and execution of theoretical demands than the proposition of the lecturer to make a distinction in connection with sanitary treatment between healthy and suspected persons coming from a center of pestilence, and, if I have understood him correctly, to desist entirely from the customary disinfection of healthy individuals. I salute with thanks one point of the discourse—namely, the request to look calmly into the face of the imminent danger, altho I am not able to share his opinion that this comfort to us results from the discovery of the comma bacillus and from the measures rendered feasible thereby. I believe, above all, that the demands made by modern hygiene in so-called contagious diseases more than grossly neglect the virtues of neighborly love and humanity, and exact and

¹ 70. Jahresbericht der schles. Gesellschaft f. vaterländ. Cultur (über das Jahr 1892), Breslau, 1893.

accomplish encroachments upon personal liberty such as can not be improved upon for malignity. Even with the conviction that the individual must make a sacrifice to the community, we can not help feeling deepest regret when contemplating the protective and defensive measures taken in the supposed interest of localities not yet infected. Hospitality is denied to all fugitives, even to the healthy. Healthy and diseased individuals are forced to leave their dwellings, and to subject themselves to procedures which even the adherents of disinfection must regard as exaggerated and, above all, useless. The fear of infection has been so overdone on the strength of the so-called bacillary theory that the results of this fear become everywhere manifest in the most disagreeable manner. But I do not wish to enlarge any further on this point. Let every one place himself in such situations as are so drastically depicted in the daily papers, and it is likely that he will recoil from the severity of the requirements of modern hygiene. What are the consequences of the present theory? As the bacillus thrives in moisture, it may adhere everywhere, and any one coming from a suspected locality, whether healthy or diseased, is suspected, therefore, to be a carrier of the infection, for he may carry the generator of the disease on himself, with himself, or in himself. From this should follow that also the healthy must be cleansed and disinfected until every fear of transmission has vanished. However, no one dares say how long this possibility of infection may last. Since, for instance, in a fatal case reported from Berlin, which is claimed to prove the connection of the disease with infection from Hamburg, the symptoms of the affection, according to my calculation, have remained completely

hidden for at least six days, a strict quarantine of at least seven days should be enforced for all persons coming from a suspected place, for, as stated above, even a healthy individual may carry the germ in himself or upon himself. But even the lecturer does not wish to draw these conclusions, and, therefore, he distinguishes sharply between suspected and healthy persons. He considers the superficial disinfection as practised in the latter to be entirely unnecessary, if I understood correctly, whereas he would submit the suspected to isolation and to energetic disinfection of the body, not only of the garments. Here we have the inconsistency between theory and practise; for, if the bacteria are the cause, then quarantine should be strictly enforced in the healthy and in the sick, in such a manner as is practised only in the Orient and in transmarine ports. If, therefore, the disinfecting measures employed so far concerning the clothing and the baggage, the insufficiency of which was so drastically depicted by the lecturer, are of no avail, if an apparently healthy individual may carry bacilli within and upon his body, then it is positive that generators of disease must have been carried away in large quantities, in spite of all measures and considering the fact that, notwithstanding the latter, a great many persons escape disinfection. Since Hamburg is a focus of epidemic, since bacilli are so readily taken up and transmitted, it would be wonderful indeed if only the few persons actually affected had been the carriers of the contagion. But since, fortunately, we have remained free from endemics and epidemics, the conclusion appears to be justified that either the bacilli are transmitted only by the patients, or the bacilli are by no means the only or the essential cause of the disease. At all events, the

opinion that they are exclusively the cause of an epidemic has not as yet been properly supported. If we boast that our measures, just because we are able to suppress every individual case, have also prevented the propagation into an epidemic, we are guilty of conclusions that may be pardonable but are none the less wrong. We have not been exempted from cholera because we have isolated a few persons and disinfected a *fraction of all concerned*, but because the requirements essential to the affection and to the epidemic in general are not present with us. The so-called sparks could not kindle a fire because the susceptible ground was wanting, because our conditions of existence do not as yet furnish any cause for disease and, let us hope, will not furnish it. If a fire which breaks out in a village with thatched roofs remains confined to the original center because the roofs are still wet from a previous rain, no one will claim the merit of having saved the roofs that were spared in that he extinguished all the sparks which were flying around; for every one knows that wet roofs will never take fire. These same facts apply to the cholera epidemic of the present year. Italy, always visited by epidemics, is spared without our having heard of any extraordinary measures, altho France probably was infected throughout the entire summer. We have been spared, not because of our measures, but because the conditions for the origin of the disease are not at hand and, let us trust, will not be. Whether we believe in the action of bacilli or not, the facts prove that, even assuming this possibility, a whole series of preliminary conditions must be complied with before the much-dreaded bacillus can do its pernicious work. I can not here enlarge upon the reasons which have led me to attribute only a very sub-

ordinate importance in the origin of diseases to bacteria, the same as to other harmful agents. I have on other occasions dwelt more exhaustively upon this subject. At present, at the risk of being designated unscientific, I wish only to give expression to my conviction that, while it is true that the causes for the origin of cholera are as yet not cleared up, it is quite safe to say that no specific pathogenic agent is the cause of this scourge of humanity, whereas a microbe is present, at best, as an accompanying phenomenon in a number of the most severe cases. It is my conviction, further, that a direct infection from one human being to another, especially in non-infected localities, never occurs, and the danger of infection in infected localities obtains only because every one in such localities is more or less subject to the external influences which are the cause of the disease. The danger clings to the locality and to the conditions of life in general, not to a specific contagion which, like other noxæ, can play only a secondary part. As little, therefore, as there is danger of being infected from a patient, so little are we justified, according to reported (unobjectionable) investigations, in accusing a definite noxa—for instance, water—of being the sole cause of the affection. The endeavor always to find the pernicious cause in water corresponds less to the compulsion of facts than to the desire of presenting something tangible as the creator of all evil. But it is a serious matter to assume absolute knowledge when every reason exists to search for truth without prejudice. There can be no doubt that water may harbor noxious substances, but these are quite insignificant so far as they affect healthy human beings. It is especially unjustifiable always to consider bacteria the carriers of the noxious element,

since there can be no doubt that chemically acting substances, demonstrable by chemical methods, play a very important part in the injury which may eventually come to man through the drinking of water. Lately the method has been adopted—wrongly, according to my opinion—of declaring water as harmful or harmless merely on the basis of bacteriological investigations because, in searching for tangible—*i. e.*, easily demonstrable—pollutions the great influence is overlooked which is exerted by the constant summation of minutest noxious elements as regards our conditions of life. At any rate, caution is necessary here, too, against one-sided appreciation of the demands and achievements of bacteriology as compared with the results of chemical tests. I am fully aware that these briefly discussed views are not shared by this assembly, because they are not in accord with the dogmas of a modern trend which lays claim to absolute reliability. But this can not prevent me from expressing my conviction that

- (1) Modern bacteriophobia leads to a neglect of the laws of humanity and neighborly love.
- (2) It nourishes the fear of infection in a most deplorable and threatening manner.
- (3) In its final consequences it leads to serious molestations of the individual and of the community; and
- (4) All sacrifices asked and made are not in proportion to the correctness and demonstrative power of the views on the basis of which they are demanded.

The course of the epidemic so far as it took place in Europe offers ample proof to those who mean to look upon matters without prejudice that the discovery of the comma bacillus explains neither the course nor the

character of the affection in a sufficiently certain manner, and for that reason that it is made the sole basis of incisive measures. One may be a true friend of hygiene which endeavors to improve the conditions of vital importance to man, and yet be forced into a position to take up arms against that direction of hygiene which, as bacteriology, undertakes naught but a battle against bacteria.

Professor Dr. Flügge: The views of the preceding speaker have really astonished me not a little. They were not so rare a few years ago, but in the course of the last decade nearly all, even those of the Munich school, have been converted. This has been accomplished in part by the discovery of the bacillus, but principally by the fact that a number of epidemics were carefully observed. Endeavors were made to harmonize the conduct of the bacillus and the epidemic, resulting in conformity in almost every particular. The epidemiological investigations were made by Koch in India, those of the Austrian epidemic were undertaken by Gruber, and exhaustive discussions took place in regard to them at the Hygienic Congress in Vienna. I desire to ask Professor Rosenbach whether he is thoroughly familiar with all the reports and discussions. Should this not be the case, I could understand why the gentleman is still retaining the old standpoint. But if he has read them, I must renounce all hope of ever coming into harmony with him.

Rosenbach: I predicted that I would thus be reproached. I have read these articles, and read them entirely without prejudice. *I regard as wrong the stress which is placed upon the fact that the bacteria alone are said to be the cause of producing all evil. My opinion will generally prevail in the future.* I speak here, also, of other epidemics than those of cholera, and I maintain that the theory of infection remains a large-sized X and an interrogation point. In Breslau we see the abrupt extinction of scarlatina, measles, and diphtheria; suddenly the curve

rises again, and we have the most distinct epidemic in spite of all reports of cases and measures of disinfection. The great X has remained as before. This is not the place for a scientific discussion of the subject, but I am ready to do so in private and in writing.

II¹

I wish to recommend still another remedy which, unfortunately, however, can not be prescribed from an apothecary—namely, the conviction that *cholera is not an infectious disease*, and that the patient does not endanger his surroundings, or, in other words, that no more danger exists in a locality in which an epidemic is present, in the neighborhood of the patient, than in any other locality. If this conviction would become generally prevalent, measures of disinfection could be dispensed with which blame the patient as the sole cause of the affection, and thus necessarily repress all sympathy for the sufferer in the interest of self-preservation. Not the patient is the center of the evil, but the conditions—unfortunately, unknown as yet—of our environment, of the climate, and of the soil, which create one region and one continent a cholera locality, and finally render the human organism unable to preserve normal functions under unfavorable conditions. What I have stated during the first epidemic of influenza regarding the non-contagiosity of this affection, then generally regarded as contagious, I maintain to-day in regard to cholera.

But until this view is generally acknowledged, fear of bacilli will cause many a heart to beat in trepidation which

¹ From an open letter to the editor of the *Berliner klin. Wochenschrift*, 1892, No. 36 of that journal.

kept its tranquility in the presence of hostile bullets, many a malodorous sacrifice of carbolic acid and calcium chloride will be offered to the idol of bacillary infection in superstitious veneration, and fumigation will take place where, according to our superstition, we assume the seat of the idols to be.

I trust that you, dear colleague, altho I know you do not share my opinion, will, in the customary objective tolerance of foreign opinions, accord space to my deductions. They may be subjective, it is true, but they have grown from experience, and, after all, I am the one who is responsible for my contentions. Let the watchword be: "No fear (hence, no disinfection), but the creation of favorable conditions of life and nutrition."

III¹

You put my self-command to a severe test, in that you unceasingly offer the most enticing "actual" subjects for elaboration. The theme now presented is also very tempting, but I decline, not without regret, but for well-considered reasons, a discussion of the question of protective measures in epidemics, and especially in cholera.

Altho the opinion may be upheld with great authority that an epidemic of cholera is likely to occur in Germany during the present year, and that the year 1893 will probably again be the year of testing all theories concerning cholera, and all performances of modern hygiene—so far as it is congruent to the doctrine of the combat against pathogenic organisms—still, prophesying is a thankless task, whether the predictions come true or, as we must wish in our station as physician and as a human

¹ Open letter to the editor of *Deutsche Revue*, 1893, January number.

being, remain unfulfilled. But these opportune considerations would not prevent me from presenting my views, quite as little as the fear of disturbing by such gloomy prophesies the tranquility of those that at present breathe freely. For, as the destruction of the germs of disease, according to the views of the now prevailing school, is equivalent to the destruction of the cause of disease, thus securing absolute protection from the pestilence, calls of alarm can tend only to arouse increased vigilance and to enhance the readiness for battle. Be it remembered that the fear of infection last year was utilized as the principal means of stirring up vigilance, and the same fear will in the future be considered an essential requirement of readiness for combat.

What restrains me from discussing the theme of the prevention of pestilences in view of a possible epidemic is not, therefore, the dread lest I alarm, perhaps unnecessarily, minds now at rest, in consequence of the apparent cessation of the malady and in consequence of the reliance upon the trustworthiness of our measures, but the knowledge that my views of the nature of epidemics and of the process of infection are far apart from the certainty of theories in which the predominant school has faith, and upon the basis of which it believes itself to be in secure possession of the means for repelling any pestilence. I would be obliged to confess frankly that, in my opinion, neither by quarantine measures, nor by antiseptic deeds, nor by bacillary investigations can we obtain an influence upon the malady (*i. e.*, are we able to prevent either its outbreak or its spread), and that those who believe in the feasibility of this view can triumph only so long as no pestilence actually exists—just as those who conjure a storm by some form of incan-

tation are considered helpers and deliverers only so long as no lightning or no hail actually appears on the scene. Now, since a large part of humanity, whether laymen or representatives of medical science, have hopefully retained the childlike belief in human omnipotence, and are certain that against all occurrences there must be a remedy and privileged human beings (scientific and social heroes) capable of repelling them, we render ourselves and others anything but a service if we point out that the hope of warding off a pestilence by the hand of man is, *at this time*, in reality nothing else but the result of an ancient belief in miracles.

Therefore, it appears doubtful to us whether, *on the basis of our present knowledge of the laws of the origin and dissemination of epidemics*, a defense is at all possible against a pestilence such as cholera, since we do not even possess a clear understanding of the relatively simple question of infection, especially of the manner and the method of the infection.

But the attempt to stifle an epidemic in its incipiency must appear still more difficult to those who look upon disease, and pestilence in particular, as a special phase in the struggle for existence between living organisms, or, more correctly, as the effect of the influence of laws still unknown to us which regulate the existence of the different species of organisms. Whether we assign to the micro-organisms a primary place in the origin of all infectious diseases, and in particular of epidemics, or, as I do in many instances, assign it only a secondary one, the affection of a single individual, and its dissemination over social connections of the latter, will always depend upon certain relations between the person affected and the pathogenic agent, and in the position occupied by

me in reference to these subjects it is a question of the decision of the important preliminary points: Whether a primary weakening of one organism only makes the latter a nutritive soil for another one; whether a special favoring of the vital conditions of the pathogenic agent only renders it aggressive for the majority of human beings; whether, further, what is injurious to one might not at the same time prove advantageous to the other. It was a question, finally, to decide whether or not micro-organisms play an essential (causative) part in all so-called infectious diseases, and whether in many cases merely a certain injury (change) of the conditions of life (in the widest sense) suffices to produce a certain pathological picture in many human beings simultaneously or in immediate succession (epidemic), without calling for the cooperation of micro-organisms; for the terms "epidemic" and "infectious disease" are not congruent.

It is quite conceivable that the measures to combat diseases depend upon the answer to this question—*i. e.*, upon the theory of the school—and that he who inclines either to one or the other of these views must hold essentially different opinions regarding the possibility of infection and regarding protection from infection, and, therefore, in active practise he is bound to oppose the contrasting view as directly harmful. If, for instance, cholera is not an infectious disease, as I believe, it follows that the belief in infection, the worst consequence of which is the *fear of infection*, is one of the most harmful elements, since fear undermines the resisting power of the organism, which should be doubly fortified by just these changed conditions of life which constitute the true cause of the disease—predisposition to affection. If we assume, on the other hand, that the germ of disease

is transmissible from lifeless objects or from a diseased human being to a healthy one, then it is necessary to keep this fear alive as much as possible, so that the carrier or transmitter of the germ be by all means avoided, and that the *only possible ground* for transmission may not be given by carelessness.

But since it is positively proved by thousands of examples that cholera is not infectious—certainly not in that sense that an *epidemic* could demonstrably be caused merely by transmission; since, further, according to the past course of events, even the opinion may be upheld that *the microbes are only an unessential* but by no means a characteristic accompanying symptom of *cholera*—it follows that the means employed at present to fight the epidemic of cholera, or even the claims to have vanquished it, must appear as entirely illusory, and effective only in that they give rise to the belief in the ignorant and in the timid that something was being done in their behalf. However, this advantage is more than counterbalanced in that the means employed render the timid still more faint-hearted, and deprive us of the possibility to see at all clearly in such complicated matters.

A defense against an epidemic is at present impossible, according to my opinion; merely a relative protection is possible in a certain sense by general hygienic measures carefully prepared in advance, and these do not consist in the practise of antiseptics and in the search for bacilli, but in the fact that *the level of the conditions of life is considerably raised, dwelling-places and food are improved, energy and courage are stimulated, etc.* Even then nothing would be attained against the epidemics which decimate the poorer classes of the population but improved resistance, for we can readily observe that

good nutrition and clean dwelling-places alone do not offer protection, since other epidemic diseases, such as scarlatina, diphtheria, etc., affect also the so-called better classes.

But such skeptical and "not sufficiently smart" opinions must not be openly expressed to-day, for we much prefer to devote ourselves busily to a blessed error than listen to the doleful truth that we do not possess a *trace of knowledge of the inherent operation of matters* in the most important questions. The consequence of this lack of firmness and this overestimation of our intelligence, when this perception is once forced upon us, is unfortunately instrumental in nearly always causing a collapse of all hitherto acknowledged principles, since those who have most fervently and trustingly implored a saint or a hero for a miracle, are most readily inclined to destroy or desert him when he refuses his aid.

The result of this view is that also with us, if we should during this year be visited by an epidemic of cholera which spreads in spite of manifold protective measures and restrictions of traffic, a victim will be sought and found upon whose shoulders the responsibility for these shattered hopes must be laid—unless previously the view should obtain that the appearance of epidemics is dependent upon factors upon the occurrence of which we have no influence, that a power of nature as yet unknown to us creates the conditions which favor the outbreak of a pestilence, and that an epidemic does not make head-way as an enemy, through an unguarded gate, slips into a fortress.

Should you, my dear sir, ever find the leisure, in spite of the limited time at your disposal, to read my article

on "Infection, Fear of Infection, and the Bacteriological School," you will become acquainted with my attitude toward modern hygienic practise which no longer discusses open questions, but considers them absolutely closed, and forces its theory as an inflexible dogma upon the manifold conditions of life. Then, I trust, you will agree with me that I do not intend, with such views, any longer to preach to deaf ears. What is a piano without a sounding-board? And the resonator, public opinion, is not so readily put in motion by deductions which urge skepticism and continued, uninfluenced, and unbiased investigation as by prevailing theories which not only come forward with the pretense that they should be regarded as "wisdom's final conclusion," but which also pretend that they have already attained the enticing aim of the delivery of mankind from the plague of epidemics.

The time is still distant in which "the laws of pestilence and war" will be considered from the view-point of the struggle for existence or, more correctly, as an expression of the law of development of mankind. And altho we have as yet not even found for these laws such a formulation as for certain atmospheric changes, we indulge in the delusion that we already possess sure means of relief, whereas in the realm of meteorology we have not yet progressed beyond storm warnings and beyond the determination of the atmospheric changes that are likely to be expected during the next few hours. . . .

XVII

SHOULD DRINKING-WATER AND MILK BE STERILIZED?

It is my opinion that chemically demonstrable substances in the water may form the cause of sudden manifestations of disease or of gradual disturbances of nutrition in the human body. The fact that until now we have not succeeded in producing symptoms of poisoning in animals by organic residues obtained from water is merely a proof of the uncertainty of pathological experiments, and I submit that, if we were to infer from this the absence of toxins in water, one would be compelled from the bacteriological standpoint to admit also the harmlessness of the comma bacillus, because the experimental ingestion of the same did not as yet produce the picture of cholera even in man. The requirements for practical purposes are in no domain so dependent upon the prevailing theory as in that of the supply of normal drinking-water, and that is why the demands of theorists and the objections to them can never be so concisely expressed as in assuming the bacteriological standpoint when discussing the question of drinking-water. Any one who regards pathogenic bacteria as the cause of certain diseases is bound to insist that *water be absolutely free from germs*, and no efforts can be too great to enforce this end. But then it is incumbent upon the representative of this theory to prove (1) that the micro-organisms accused by him are really the *sole cause* of the affection, and that they are principally absorbed with the

drinking-water; (2) that all such pollutions are to a certainty excluded by the use of wells which utilize only the ground-water; and (3) that the fulfilment of the requirement of absolute freedom from germs does not create other noxæ, which more than balance the advantages of the exclusion of pathogenic organisms. I shall not dwell upon the first point, as it was exhaustively discussed in a session of last summer, and I wish only to emphasize that, altho I do not deny that there are diseases which are produced by micro-organisms, just regarding the two affections which are principally traced to the use of injurious drinking-water—namely, typhoid fever and cholera—I profess the opinion that the so-called specific bacilli play no part, or only a very secondary one. I neither deny that diseases resembling typhoid fever are occasionally caused by the drinking-water, nor do I dispute that bad drinking-water, in times favorable to the development of cholera, may give rise to a disturbance of the function of the intestine; but I deny, upon the basis of my experience, that the drinking-water is the real cause of typhoid fever and of cholera, of their endemics and epidemics, in the overwhelming majority of cases. The fact that water is continually accused of being the cause, and that the decline of the disease after the closing of the well, which usually is not done until the *epidemic has reached its acme*, is attributed to this sanitary measure, can not for me and for many others take the place of a scientific proof of the etiological connection. Now, let us question further. Do wells, even of the most recent construction, actually guarantee the impossibility of pollution, and is there absolute certainty that the ground-water always furnishes a water better in every respect than that supplied by our excellent water-

works, which did not fail even during the hot summer of the present year? I believe that this question may not at once be answered in the affirmative; for wells may be polluted at their outlet opening, and the ground-water may also, under certain circumstances, receive pollutions which then will pass into the well. Besides, if a well is polluted, the danger to the consumer is greater than when a pollution reaches the much more powerful current of the river water, the filter of which afford a certain additional protection. Even when urging from the standpoint that *infection by drinking-water*, be it obtained from a well or from water-works, does not play an essential part, or even if we do not oppose to well-water (just as I am in favor of it), the question arises whether it would be well, for the sake of a theory, to advise the acquisition of a new water-supply, without regard to the enormous cost involved, and possibly at the same time awaken doubts in the minds of the people as to the excellence of our water-supply? The catchword of well-pollution has always wielded a great influence in times of excitement. Finally, with reference to the prevailing tendency to render *everything free from germs*, I wish to give expression to the medical doubts whether the production of germ-free food-stuffs might not be accompanied with some disadvantages, since it requires a complete renunciation of the useful activity of the microbes. And such an activity unquestionably exists; for we are familiar with the great rôle of division of labor in nature, and we now know that so-called symbiosis—*i. e.*, the condition in which two forms of living organisms are interdependent upon each other for their existence—plays a prominent part everywhere. Thus there can be no doubt that the *normal digestive activity* in the intestinal canal in a

wide measure depends upon a symbiosis, in that the micro-organisms absorbed with the air and with the food usher in and maintain the splitting up of the food in the intestinal tract, and thus materially facilitate the real labor of the tissues of the body. Hence it is probable that the organism, especially at times of marked activity, can not dispense with the assistance of these bacteria and must manifest disturbances as soon as these cooperators are entirely withdrawn from it by means of sterilization. If, therefore, the ingestion of sterilized food may be of advantage to some individuals, it is quite as certainly harmful to others, and, accordingly, the physician must strictly individualize here too. For this reason I must not fail to emphasize here that a series of observations of myself and of others appear to point to the fact that, for instance, *sterilized milk*, the utility of which I do not misjudge, causes digestive disturbances in many children, which are either due to a special change of the albuminous bodies during sterilization, or, which is more probable, to the destruction of all the micro-organisms of the milk, even of the most useful. Let me also call attention to the fact that the ingestion of boiled water, even when sufficiently cooled, is not always beneficial for digestion, especially when it is a question of drinking large quantities during the hot season and by individuals with weaker digestive organs. All these reflections deserve consideration before deciding in favor of an expensive change of the water-supply in a one-sided adherence to bacteriological requirements. This seems to be especially important because the always timid population would be particularly frightened by an allusion to the deficiency and danger of our water-supply which can not at all be shown to be present.

XVIII

INFECTION, FEAR OF INFECTION, AND THE BACTERIOLOGICAL SCHOOL

SINCE nothing renders life and activity more questionable than disease, and since daily experience appears to teach that the most dangerous diseases are remarkably often transmitted from man to man, it is quite obvious that we entertain a special fear of this treacherous enemy, infection, with which a relative, a friend, or fellow man with whom we are in close connection may maliciously be threatened. But it is unquestionably surprising that just at present, in this era of greatest daring and personal courage which often is ready to stake life for mere trifles, the fear of infection is so exceedingly pronounced. Health and life are risked every day in science, in play and in sport, by investigators—who, like a sorcerer, keep the evil spirits under lock and key to force them to work for the benefit of mankind—by serious explorers, and by mountain climbers, not to mention those who, even on the strength of a most singular sense of injured honor, prove their disregard of life—frequently, it is true, only that of the opponent—in a duel. If, then, in a remarkable but psychologically conceivable contrast, a form of heroic, or, let us say, blind, contempt of death in attaining ambitious aims, and pale fear, or, what sounds better, overcaution in the intercourse with diseased fellow men, are the sign manual of our time, then the fear of infection must of neces-

sity be a very peculiar form of psychical influence, and the investigation of this problem must be particularly suited to shed a bright light upon the views of a generation, upon the psychology of the mind of the people, since we always assume that humanity is seen at its best just in the nursing of the sick and in the intercourse with patients.

In fact, paradoxical as it may sound, the particular manifestation of this fear may possibly contain a certain flattery directed at our address; for we only pay a compliment to the extent of our knowledge if we say that our fear arises from nothing but the recognition of the truth. To avoid a clearly recognized danger is caution, not fear, and caution, as is well known, is the better part of wisdom. Whether, guided by fear, we arrive at cruel conclusions, in that we exclude from society patients threatening our persons as we would the socially diseased, the criminal, and the morally depraved does not come into consideration, since modern time has taught that the rights of the species are far above those of the individual. This would explain the fear of infection as the necessary prudence in the presence of a clearly recognized evil, against which we are able to protect ourselves, according to the progress of science, with certainty only by avoiding all contact, hence by shutting off the source of danger, because the carrier of the danger is a human being (respectively what has been touched by him) whom we can not unceremoniously render harmless in slacked lime or in a flame, such as is done with lifeless objects or animals which we regard as the carriers of infection; for example, rats, which are looked upon as carriers of pest.

One of these reasons may be found in the fact that the official acknowledgment of heroism has become an easier

matter than was formerly the case, owing to the rule of publicity and to the growth of advertising. If the whole of ancient Greece solemnized one or more victors every four years, the entire world now solemnizes daily victors in all domains of physical activity. The greatest activity is the greatest glory. But glory can at this day scarcely be acquired in conquering fear of infection; for just the profession of the medical practitioner, the quiet heroes of this victory, gained day after day without vainglory, has greatly suffered in esteem—yes, its moral standard is rated especially low, as is shown by the call for strict disciplinary laws. Or should physicians be considered cowardly because they now demand scrupulous measures for intercourse with infectious patients?

That such can be the case teaches that our period has no room for silent deeds of heroism or for more passive (mental) heroism. Only the noisy, active (physical) heroism counts, and it is conceivable that the thought to be ill without glory is much more difficult to bear just to very daring minds than the one "to die in beauty" or to lose a limb in battle. The invalids of a combat are always surrounded by a greater halo than are the cripples of peaceful labor or even those of disease.

Another point is in connection with what we have stated above, with the pride in the progress of our knowledge. So long as infection was looked upon as something mysterious, and very many diseases which today are regarded as infectious were not considered such, fear was also present, it is true, but only of patients who showed great destructions externally, and only in greater epidemics, in which infection or its consequences were apparently tangibly horribly manifest. But now that

science has solved all problems, that we know the danger and its causes, that not only the patient, but also his atmosphere, his clothes, his intercourse, harbor the certain danger; now that all diseases have become infectious, fear, or, let us rather say, caution must be especially laudable. For we are not able to conquer disease or the patient by our strength or by the power of our body, as we can a real adversary or realistic nature. It is true, it has been maintained that the bacilli were "sedative" bacilli, since the determination of their presence also afforded the possibility of battling with them. But practical success did not, in our opinion, confirm the certainty of this conclusion. And thus the watchword holds good: Disinfect externally, but protect yourself as much as possible from intercourse with the suspected. Caution is necessary, therefore, because thus the medical results and the progress of science are duly considered, and this I regard as a second point to characterize our period which, on the one hand, is daring, and, on the other, trusting in authority, especially credulous with reference to the progress of science which has created many new facts or new problems, but no new or important perception in the realm of medicine, as the adherents of the modern trend and of the negation of all facts of experience would have us believe.

If we thus perceive that even physicians entirely neglect clear observations of former periods and at once accept new scientific achievements, and, strange as they may be, apply them in practise because their originators have acquired fame by labors which may perhaps deserve recognition in the domain of pure theory or under limited other view-points, or because they bear the stamp of professional authority, it is conceivable that this trust in

authority is readily transmitted to the laity, especially as it may attain particular prevalence by laws which can readily be enacted in accordance with the tendencies of the dominating trend.

If, in my opinion, the various epochs of the history of mankind or of the history of culture are differentiated not so much by external occurrences, but rather in that the norm of thinking, of the conception and judging of ethical and practical subjects are, *a priori* as it were, from the bodily characteristics, different in the different generations, for reasons which we need not investigate here; if we consider that, according to the rule designated by us as the law of contrast, the following generation usually forms the opposite of the preceding one; if we may look upon the main passions and upon the main anxieties of a period as the most important symptoms of the trend of thought, as criterion for the cultural standpoint, then considerable importance must be attributed to fear of infection so markedly developed to-day. Let me call attention to the middle ages, during which this fear also had attained a very marked expression; to the middle ages, during which it was also believed that the causes of all bodily and mental ailments were recognized with certainty, in that the causes for the latter were looked for in witches and sorcerers; for the former, as is the case to-day, in the poisoning of wells. Thus it was possible for well-meaning persons and for the authorities of science, on the basis of the science of that day, to attempt to exterminate all infections, in that they, in charming harmony with the minds of the people, tortured and burned witches and poisoners of wells. The fear of disease, and especially of infectious disease, is always particularly great in periods during which ex-

cessive significance is attached to the body as against the soul, and during which the most evident manifestation is represented as the most correct, or the true, cause. Let us now examine how fear of infection has gradually developed.

The German language has two definitions which, in the most subtle manner, enable us to express our opinion as to the appearance and the nature, the exterior and the contents, of objects with which we come in contact. We call "*rein*" (clean, pure) all objects that, according to their nature, to the contents, are considered the most perfect of their kind; "*sauber, reinlich*" (cleanly) those objects the surface of which does not show any trace of a foreign substance adhering to it, hence, which shows the original substance—at least, externally—in its cleanliness. The equivalent of clean in old high German means "sifted," "bolted," hence, expresses the uniformity and excellence of the material, whereas the word "cleanly" signifies only as much as stainless. Mankind in its various races, however they may have differed in their individual views, from antiquity on has always adhered to the conception of "cleanness" as a binding fundamental principle for certain clans, and it is not an uninteresting glance into the history of tribes to follow these views regarding the conception of cleanness through the history of peoples.

The conception of cleanliness, strangely enough, was entirely relegated to the rear in the most ancient nations, in whom the conceptions of "clean" and "cleanly" referred only to physical relations (the conception of cleanness, purity of the soul, was not created until later); only in general were certain substances and certain actions designated as clean or unclean—*i. e.*, as fit to serve

as a symbol of the relations to the highest being. It was impossible that the conception of cleanliness could properly obtain with peoples whose external habits and conditions of life were the most simple and unfavorable conceivable. The Oriental nations who traveled about in desert lands, and to whom water was a costly possession, could not possibly manifest external cleanliness in its most perfect form, and thus it was that a symbolic cleansing of some part of the surface of the body—for instance, the mere sprinkling of the hands with water—sufficed to satisfy the demands of external cleanliness, whereas so much more stress was laid upon the rigorous observation of certain external signs and precepts which justly or unjustly were regarded as symbols of internal cleanness and as pleasing to the Supreme Being.

Thus a restriction of the conception of "cleanliness" to "internal cleanness" had occurred, and the conception of uncleanness—*i. e.*, of "external cleanliness"—became less prominent or received a different interpretation, in that even the donning of a certain garment was considered a sign of external cleanliness. However, the more objects as such were from the beginning stamped as essentially different—for unclean was equivalent to "not fit to use" and worthless—the more a difference of classification according to the conceptions of clean and cleanly became manifest also among men. Any one who aspired to be considered a person of prominence, could accomplish this only in that he imposed certain restrictions upon himself, and in that he declared certain objects to be uncleanly for use which, to other members of the tribe, were still cleanly, and in this manner, if he succeeded in asserting his views, he degraded the others to unclean—*i. e.*, to beings of a lower order with whom he

could not have any intercourse. Since a vanquished tribe usually differed greatly in its habits and religious customs from the victor, it is obvious that here, too, through the powerful influence of religious institutions and precepts, very soon a deep gulf was opened between the clean and the unclean, and henceforth the conception of caste was created. The dominating class could hold its own only in that the others believed them to be something better and nobler (*i.e.*, something "clean"), and the king, the noblest of the noble, the cleanest of the clean, was separated from his subjects in a form that was likewise sanctified by religion, like a being of a higher order, rendered unclean by the mere glance of a lower being.

Any one who even externally exhibited the characteristic of uncleanness as a sign of disease, or on whom nature had imprinted an external blemish, was expelled as unclean by the whole community, and even the lowest of the unclean, but healthy, had the doleful consolation of beholding beings more despised than himself. Even the pariah could feel himself above his still more miserable brother.

This gulf was bound to persist so long as a certain difference of matter was considered characteristic; it was obliged to disappear at that moment in which the nature of man was found to lie, not in his external form and in certain outer marks, but in expressions of the spirit or of the soul. If the spirit and its cleanness were the essential, then the body and its composition were the transient, unessential, and all men were equal because every one possessed a soul and might struggle for spiritual cleanness. Then it was immaterial for estimation whether or not a person was sick or miserable; in fact,

the miserable, the afflicted one, even appeared enviable, because he possessed the nearest claim to have his spirit delivered from the unclean matter in death.

But the teachings of Him who did not repulse even the leper could not lead to an equalization of men during life, because the body was the ballast which held the flight of the soul down to earth and clouded its cleanness. An equalization of souls, therefore, could take place only after the severing of the soul from the body, and only under the presumption of a cleansing from the influences of matter; and thus, in a one-sided development of the idea of the unworthiness of matter, a point was reached at which matter was valued so low that it was considered a privilege to destroy it as rapidly as possible, and, by neglecting all measures intended for its natural preservation in the form of the body, to restore it to dust as speedily as possible. Thus there had occurred, instead of equality of man, only a reversion of the former conditions: formerly, cleanness of *matter* was esteemed; now, that of the *soul*; and, since cleanness of the soul will become the more gloriously manifest the less value is attributed to matter, the conception of "uncleanness" of the body of necessity was bound to disappear entirely; certain anachorites of all systems of religion have most drastically illustrated this. However, the longer the people were preached that the body was unclean, the more they were inclined to consider external beauty a sign of cleanness; for as ordinary man can conceive the soul only as matter, he must necessarily associate with the conception of higher cleanness of the soul the conception of a higher, nobler matter, and he will arrive at the conclusion that, with an enhanced cleanness of the soul, matter also would become more clean—the ignoble

matter of the body is altered, ennobled, by cleanness of the soul; it is, as the German expression strikingly defines it, "*verklärt*" (transfigured).

Thus the opinion began to prevail (this feature can be shown also in the art of painting) that a graceful body was a sign of a clean soul, and that the ennobled outer form was bound to exert a favorable influence upon the cleanness of the soul; external beauty began to find favor, and endeavors were made to beautify the external form. This endeavor naturally went hand in hand with the fear of everything that was not beautiful; yes, people began again to look upon the externally visible signs of destruction of the body—*i.e.*, the external diseases—as the visible expression of internal uncleanness, as a sign of heaven, through which an unclean soul externally manifested itself, and thus fear of everything which deviated from the usual form (the horror of foreign, incomprehensible habits, of external injuries, yes, even of—for extremes will touch—unusual external beauty, behind which lurked the tempter) began to become prominent again.

But, above all, fear was dominant of contaminating their own body by contact with others whose bodies were unclean—especially the bodies of the sick, of lepers, of the victims of pest; and we learn from the history of pestilences that not only special buildings were erected for lepers, but that a brother would expel his sick brother, that all ties of family and friendship were loosened in times of pestilence. The enemy was suspected everywhere: the air, the wells, food, human beings—all were believed to be the seat of the evil spirit ready at a moment's notice to enter into every clean body, and to carry bodily and spiritual ruin in its train.

A contradiction could be formulated from the fact that human beings, anxious only regarding their spiritual welfare, were afraid of contamination of the body; but we must bear in mind that the conceptional faculties of the masses already looked upon the soul as something purely corporeal, and, therefore, were bound also to assume a bodily contamination of the soul as possible and probable; in fact, many pictures represent the soul as a corporeal being in the hands of infernal creatures.

As it is the highest ideal of those who consider the essence of man to be a harmonious blending of soul and body, to acquire this harmony, to see highest cleanness of soul embodied, so, in the era of materialism, which denies the influence of certain imponderables upon life, this aim has been lost sight of. We have again reached the point of giving an absolute realistic definition to the demand for cleanliness of the body. We might even be justified in maintaining that now we look upon the mere cleanliness of the form or of the vessel which, according to the opinion of idealists still existing, contains the soul, as the essence of cleanness. And since external cleanness is identical with cleanliness, we might possibly contend that we are now too much inclined to regard cleanliness as the first characteristic of a noble or clean human being. This language may, perhaps, appear exaggerated to some; but any one who is aware that the outer clothing, the form of the beard, clean linen, a certain shape of the finger nails, and certain prescribed movements may suffice to stamp one as a member of the best society, will possibly admit, after all, that we are at least on the road to look upon external cleanness—hence, cleanliness—as the essence of all things. It is certainly out of the question that any one who does

not parade such cleanliness as is required by fashion in our day can not lay claim to being perfect as man, and the less our present development even is capable of attaining that perfection of the mind in reality necessary to judge of the essence of things, the more will a clean and beautiful external form be looked upon by those who are incapable of judging—and that is called tendency of the period—as equivalent to the richness and beauty of the contents.

Hence, in the development of mankind, we have passed through about the following important stages:

- (1) Estimation of the value of objects and of men according to certain arbitrarily assumed material qualities.
- (2) Disregard of the material, and high esteem of the psychical, qualities.
- (3) The belief that a beautiful soul could dwell only in a maltreated body.
- (4) The belief that a deformed body predicated also a deformed soul, that matter contaminated the spirit.
- (5) The culture of the "beautiful soul."
- (6) The cultivation of the body.

We trust that the future may to this period of materialism assign a period in which the conviction prevails that soul and body in all human beings who are not equal, it is true, but homogeneous, must be cared for in an equal manner to accomplish a certain perfection of the individual. If we return to the present, it can not be denied, indeed, that the cultivation, respectively the caring, of the individual, especially in the so-called better classes, has made rapid progress. The conviction has gradually gained ground during the last decades

that a far-reaching separation of the sphere of the individual is so essential to the welfare of the body that, even in the performances of every-day life, the community of objects in frequent use is contradictory to the principle of cleanliness. How otherwise could we explain the fact that man constantly requires more room and more objects of bodily use for his own personal wants than from the endeavor to attain a continually increasing bodily isolation. Whereas formerly whole families utilized one small room as living-room and as bedroom, the requirements are now to procure a separate living-room and bedroom to every member of the family; whereas formerly all members of the family and the servants ate from the same dish, every member of the family now has separate utensils to use for eating, separate towels, basins, etc. The aversion to bodily contact is manifest also in that even expressions of love in the family, kissing between children and parents, are continually restricted more and more; the kiss of friendship has ceased almost entirely. Our hygienic authorities tumble over one another in accusing kissing upon the mouth as the surest means of transmitting infection, and unquestionably they have been successful with their warnings among the public, with the exception only of lovers, who remain true to the eternal law of nature as against the changing postulates of science.

The endeavor to keep everything that is foreign at a distance is expressed also in other directions; we attempt to free ourselves as much as possible from the influences of our calling and of our surrounding, in that we frequently change our clothing and wash ourselves, especially the hands, altho we are not just about to take a meal or to conduct our hands into the mouth. Why do

we do this? Why do we so carefully comply with the outer forms of the requisites of cleanliness? *Because the care of the body has become to us a commandment of morals, a virtue*, because worshiping of personality requires a special cult, and because we can best express the value of our personality in that we consider it to be something of a higher standing which might be contaminated by every external contact. We manifest the cult of our own personality by nothing else but by the painstaking exclusion of all that is foreign—*i.e.*, not pertaining to our personality—by the use of separate dwellings and of separate utensils, by careful cleansing of the food, and by the washing of the hands before we are about to introduce food or drink into our body. Whereas formerly cleansing was resorted to only when coming into relation with higher beings, it now obtains when we bring objects of the outer world near to *us*; we touch everything with gloves, and disinfect everything, as it were, before bringing it in contact with our inner self.

However, this exaggeration of the cult of our own personality, as manifest in the observation of the outer forms, must naturally become still more markedly prominent when it is not only a question of the single individual, but of the welfare of the community in which the egotism of society demands its rights. This rigorosity is evident even in small towns; for it is unquestionably a symbol of culture observed by society if at social gatherings devoted to feasting or entertainment every guest is expected to appear in full dress. A garb of joy, after all, is not the same as a garb of elegance.

Therefore, to manifest the interest of the community (species, variety), the striving for external cleanliness must become still more prominent, and then it turns

against the individual with elementary force; for the greater the care and the estimation demanded by the single individual, the greater will also be the claim of the community as to special estimation and protection. Because every one, in excessive cleanliness, no longer regards the other as clean, altho the superstition that some human beings were formed of a nobler material has lost its omnipotence, because every one, in selfish egotism, shrinks from the touch of others, even if they are not diseased, in the same manner must the egotism of the community, striving to preserve the cleanness of the species, *turn with asperity against the single individuals whose physical or mental qualities do not correspond to the prevailing conception or ideal of cleanness*, since they might endanger the community on account of their deficient cleanness. Thus we see how society, owing to bodily egotism, is led to remove certain diseased individuals as quickly and as securely as possible from the society of others, to isolate them so as not to contaminate others; thus we see that even peoples separate certain allegedly foreign elements as unclean and hostile components according to physical and mental characteristics, and attempt to expel them. Race hatred insists upon *one* form of nose and upon *one* color of hair, and political tyrants demand *one* opinion among all fellow citizens.

The endeavor is directed, therefore (whether consciously or unconsciously is immaterial), at the removal of patients or of those with abnormal development—either bodily or mentally diseased—from the family and from society, to avoid any chance of contact. This endeavor in the domain of bodily disease is expressed in that the intercourse with “unclean” bodies is transferred in a continually increasing proportion upon

strange, paid persons, or also upon such as voluntarily, to practise renunciation, impose upon themselves the sacrifice of caring for the sick. In the eagerness to rid the community of all unclean elements, to guard it against the frightening specter of infection, continually more diseases are declared to be infectious and, accordingly, subject to isolation. In the *endeavor to save society at any price*, not only patients with diphtheria, scarlet fever, measles, and typhoid fever, but also the tuberculous and individuals afflicted with cancer, are regarded as foci of infection and timidly avoided, altho in several of the above-named forms of disease, especially in the two last-mentioned, there exists not even the shadow of a justification of fear of direct infection.

Thus, society, in the cruel sequence of the dogma of the value of personality and in one-sided pursuit of the aim to protect the bodies of the community as the more valuable, adds to the bodily sufferings of the patients the further torture brought about by the knowledge not only to be excluded from the joys of life, but also, without fault of their own, to constitute a constant source of alarm—yes, even the certain cause of injury to their fellow men. *Thus, the egotistic, ardent desire of the individual at any price to keep himself clean—i.e., to protect himself from infection—leads to the much more cruel egotism of the community, which, under the claim that the advantage of the common welfare demands it, can enforce the removal of all those who are unclean according to the view of the community—i.e., their isolation or expulsion.*

The certainty really to attain the desired end, the expulsion of everything that is harmful, will naturally appear the greater the more extensive *the scope of the conception of "uncleanness"—i.e., the larger the number*

of diseases and noxæ which we are entitled to consider infectious—the more cautious we become in defining the conception of what is really harmful. However, a highest authority must be found, above all, which, acknowledged as competent by all, takes charge of this definition. Society will then soon establish the laws regulating the conduct of the individual toward these “guide-posts to what is right”—*i.e.*, stipulating the punishment for infringements upon the injunctions established in the interest of the community. This last resort, which establishes the “*god of the day*,” or, more correctly, the *idol of the day*, must be created, and society must be compelled, apparently in its own interest, to acknowledge the idol as deity. This is accomplished by using (or abusing) the ideal trait in man to submit to the noble and worshipful, even if a sacrifice is required; thus, what is really venerable will gradually be replaced by a caricature of the ideal which narrow-mindedness and near-sightedness, believing themselves in possession of the truth, would be fain to pass off as truth. Thus, truth is displaced, to serve as rule of conduction and as last resort, by the idol of fashion, by the *catchword*, and by this false scale all our deeds and actions are measured.

The fashionable idol, therefore, to which man voluntarily subjects himself, is the catchword which, as a simple symbol, as a *sound-picture* that may be reproduced as desired and without thinking, imprints itself upon memory like melody. The high-sounding catchword, quite easily handled also by the non-thinking, unfortunately takes the place of the conception which can be acquired only by the act of thinking, and which causes the isolated impressions upon our senses to become our

mental property in that, aided by reason, it condenses the individual vague sensations and stimulations into the unit of the idea.

However, the striving of the mind of the people and of the individual after perfection is guided into the wrong direction or is misused by high-sounding phrases or catchwords, and this abuse is especially abetted if the egotism or the good faith of certain classes utilizes fear to derive from it a system of guardianship for the ignorant. If, for instance, one authority is empowered to define the conception of what is to be regarded as "clean" and of what is to be looked upon as "infectious," and if it is also entrusted with the execution of the protective measures according to the definition as given by it, the decision of all questions of every-day life is also placed into the hands of this authority. It is thus put in a position to direct the opinion and the actions of the obedient arbitrarily and at will—hence, to guide the mind of the people in thought and action, as it were.

Whereas formerly all efforts toward guardianship of mankind were connected with the *spiritual welfare*, and definitions without number were created to define the conception of what is unclean, and to determine the protective measures according to which infection of the soul could be avoided; whereas formerly the most innocent objects and actions were designated as injurious to the soul, so that man beheld himself surrounded by evil spirits which could be prevented from doing harm to soul and body only by certain prescribed actions, the same endeavors are now associated with the *welfare of the body*, and they attempt to draw man into their ban, in that the dangers threatening his body are depicted with the darkest colors. *Medical police and public hygiene are*

the symbols under and by which endeavors are now made to forge the old chains around the body of man.

Thus we are again on the high road, instead of establishing the *equal cleanliness* for all men, to make the preservation of *cleanliness*—hence, the merely outward sign—the aim of our endeavors, and to neglect, in so doing, the improvement of social conditions which alone are of importance. We stop half-way, in that we formulate a false ideal of cleanliness instead of giving the individual free air and space and opportunity to manifest his own individuality. The more the fear obtains that man is apt to bring harm to man, the more the egotism of the individual will compel him to separate his interest from that of others in order to isolate himself as much as possible. Dangers are invented affecting the “ego” in its contact with the outer world, and they may be presented the more conspicuously the more it is possible thereby, under the semblance of justification, to cover up the real purposes of egotistic measures. (To discuss how scientific authorities endeavor to accomplish this by mental infection, or even how police and censorship attempt to attain this end, does not form a part of our theme.)

Groundless fear of our sick fellow man, or of the dangers brought to us by surrounding nature, is always a sign of *weak-minded subjection* to so-called authority—hence, a sign of retrogression. For, so long as we forego personal investigation, we shall always be afraid of witches and gnomes and mysterious powers, whatever scientific names they may pass by. So long as we do not according to our own opinion but only in accordance with the views of others declare what is “clean” or “unclean,” “harmful” or “useful,” “good” or “bad,” the manifestation of the “ego” is impeded and progress is ob-

structed, since we do not dare to take one step without foreign aid. The more man finds himself surrounded with dangers, the more will he be inclined to follow the wisdom of those who claim to possess infallible means against these dangers. Any one who ascribes an eclipse of the sun to the action of evil spirits will be too ready to make a sacrifice to those who pretend to be able to conjure them.

Hence, just on account of the veneration which is again accorded to the body, we are dominated by the fear of infection by other organisms, or by influences of surrounding nature, and we shall be the more willing to submit to anything and everything to banish this fear, *the more uncertain we are regarding the nature of infection*. It is worth our while, therefore, to look more minutely into this fear of infection which, as we have explained above, has dominated mankind since the earliest times in varying periodicity, and to determine in how far it is justified, also in how far we possess the means of protecting ourselves from infection. We shall not banish superstitious fear and, what is more important, superstitious measures from our mind until we understand that *disease and death are natural processes, stages of the development of matter* to which nothing supernatural attaches, as little as to any other process occurring on this earth, until we see that much of what is explained as infection (transmission from person to person) can be solved in a different manner. Everything must be called superstitious that corresponds to a false belief—*i. e.*, the vanquished belief of a lower stage of development or of a deficient recognition of facts.

To infect means to cause something to adhere—in a similar manner as in igniting a fire we cause fire to ad-

here to some substance. The belief obtains, therefore, that in infection something which may bring destruction is transmitted in such a manner as we transmit fire upon an inflammable object; the conviction also prevails that the infected individual also runs the risk, as it were, of being consumed by this internal fire.¹ The popular belief always had in mind this form of transmission of harmful matters, above all, since the picture of transmitting a flame was most plausible to it.

If we hold to this example of inflaming, it is obvious that a flame must not necessarily arise wherever there is fuel, and it is quite as obvious that, even if there is fuel, it does not follow that this fuel can be utilized (for instance, damp wood). But even if we are in possession of flame and fuel, it still requires certain favorable conditions to put the flame to the fuel and inflame it, as every one knows who has ever attempted to light a cigar in the wind or a fire in the stove. Hence, several other conditions must be complied with before the inflammable material really catches fire; but even after the flame has taken hold, this does not constitute a certainty that the substance will be consumed by the flame, for the latter

¹ The fear of infection in its last analysis is in reality nothing but the indistinct expression of the impulse of development into the highest and best. In accordance with the indistinct consciousness of our having developed from lower forms of matter to higher ones, we are possessed of the fear of retrogression to lower forms and of the dissolution into more simple combinations of matter, especially of the decomposition into non-animated substance. The fear of contamination by lower organisms, therefore, can be derivatively explained as the expression of the gradual differentiation of higher forms of matter from lower ones. The conscious organism (and only in such can there actually be a question of fear of infection) endeavors to keep clean—i.e., not to relapse into the modifications of matter which correspond to a former stage of development. This indistinct self-consciousness which probably forms a powerful factor of development this vague fear of retrogression, might possibly be conceived as the expression of the "aristocracy of matter" or of highest transcendental influences.

may at once go out after lighting, or it may be confined to a very limited space shortly to be extinguished, so that even here inflammation having been accomplished does not mean a guarantee that the fire will continue to burn.

Such are the conditions in the human body. Altho a surely infective substance is present, the so-called focus of infection, it does not follow that every one who comes in contact with this focus will be infected. Let us suppose this focus to be a human being in whom, according to the modern theory, smallest organisms have colonized which, reaching the air through the sputum or through other discharges, may be transmitted, like a flame, upon an inflammable subject—another human being—here to cause similar changes as have already developed in the patient serving as the carrier of the infection. Let us further assume that this infecting patient be approached by another individual; this does not constitute a certainty that the latter will in reality become affected any more than that a human being approaching a fireplace, or the fuel near the latter, will become inflamed. A combination must first be effected—*i.e.*, the inflaming material must so be brought into proximity of the substance to be inflamed that it comes into closest contact with it—and, since an inflaming substance can as little be absorbed through the intact skin as a flame will attack the green bark of wood, the infective substance must reach the body through mouth or nose. But the mouth is usually closed in breathing, hence the current of air containing the infective material must pass through the nose, and this organ contains tenacious mucus and a number of other contrivances which filter, as it were, the air we breathe, and retain all dustlike, solid particles.

If, nevertheless, they reach the organs of the throat, they are there again retained by mucous substances, and will later be expelled by cough or by so-called ciliary movements. But if the infective material had actually passed from the patient upon the hands of the nurse, and would by the latter, in utter neglect of all rules of cleanliness, be transmitted into the mouth while eating, then the infective substance may certainly, the same as the one that had reached the organs of the throat with the air, be carried into the stomach by means of the natural movements of deglutition. But even then the body is not infected yet, for, altho the cavity of the stomach is in the interior of man, it is not his true essentiality which we must look for in the tissues proper. Besides, the gastric juice under normal conditions destroys every invader or alters it so that it is rendered harmless. Even when not sufficient gastric juice is present, even when the other parts of the alimentary canal do not functionate properly, there still remain vomiting and another form of discharge capable of forcing an injurious agent to leave the body before it reaches the tissues constituting the real interior of the organism, without an actual infection—a colonization of the foreign body in the tissues—having taken place. Transitory manifestations of disturbances will arise, but the real infection, the involvement of the entire body, has not occurred yet. And even when the infective material enters the most interior part of the body, even when it is present in the blood, still the body is not yet inflamed; the latter is still able (with a modicum of malaise) so to rid itself of the foreign body, or, let us rather say, of the foreign irritant, that the latter will not find a permanent abode.

Therefore, even after the inflammation has been suc-

cessfully accomplished, the flame can not be sustained if the material lacks combustible qualities, if something is present which prevents combustion, or if something is wanting necessary to the maintenance of the flame. Thus a material otherwise suitable for burning will not burn when it is damp: succulent grass and damp wood can not be inflamed; waterless grass (hay) and dry wood burn blazingly. Neither can a substance be inflamed if heat is abstracted from it, or if it can not be brought to a certain temperature if the access of air is insufficient, or if that form of air which maintains the process of combustion (oxygen) is absent.

We observe, therefore, that, even presupposing the *possibility* of infection through, or in the presence of, an infecting agent or of a body already infected, the *probability* of becoming affected is extremely slight for those that come in contact with the patient; it is much less than that of a soldier going to war of being wounded. If the opportunity for infection were even approximately as great as the adherents of modern bacteriology depict it, no nurse and no physician could or would expose themselves to the danger. But, as a matter of fact, we observe that *infection of those that are engaged in nursing the sick, and of those connected with them*, altho they usually do not and can not act with great precaution in their intercourse with the patients, occurs by no means *more frequently* than is the case in circles that have nothing to do with infectious patients—a fact which certainly furnishes proof that there is a wide gulf between the possibility and the probability of infection.

But now the cautious will say: Admitted that this probability is very slight, still caution is the better part of prudence, and it is best not to run the risk of be-

coming infected at all, since it is impossible to estimate one's own predisposition to infection. To this we can only reply that we do not know the form and manner and conditions of the affection, and that keeping away from patients does in the least constitute a guaranty that disease nevertheless may follow, even of the timid or cautious, and at that in a manner and by a road least expected. As in battle a bullet may unexpectedly strike also the coward, while the brave remains unhurt in spite of the hail of bullets, so the destiny of becoming affected is independent of all precautionary measures, since we only know *some of the conditions of protection*.

The best protection will always be: *Bravely to fight the battle of life, and so to strengthen and harden the body that it becomes and remains capable of resistance*. Any one who, to protect himself from dangers that he suspects everywhere, timidly retreats, and, instead of accustoming his body to the varying demands of life and to a natural mode of living, neglects it in that he faintheartedly keeps it back from all that is natural, any one who treats his skin with disinfecting agents and allows his stomach to partake only of so-called harmless food, will experience not a strengthening, but a weakening, in the struggle for existence, as a result of his incorrect actions.

If the various species of the animal kingdom have wonderfully adapted themselves to considerable changes of the conditions of life without having been more decimated than man, why should not just that being which possesses the greatest faculty for adaptation endeavor to sharpen and to perfect, above all, the natural weapons in the struggle for existence; hence, to utilize this faculty for adaptation and the possibility of rational employment of all resources for the ame-

lioration of his existence? Why search only for weapons purporting to destroy a *distinct* enemy, and why endeavor arbitrarily, certainly without positive proof, to proclaim *one* danger as the one to be fought above all others, as if this one were alone present and all other dangers offered by the struggle for existence shrank into insignificance?

Why this belief of benefiting mankind by proclaiming the smallest living organisms as its only and particular enemies, whereas weather, moisture of the soil, social requirements, and other factors essentially influencing the conditions of life are no longer permitted to play a part in the tragedy of life? Is the fact altogether lost sight of that all organic beings are influenced more than the science of the laboratory ever dreams of just by these factors, and especially because they act upon us not only under certain conditions, but with certainty and *continuously*, since we must submit just to their influence with every breath of air we draw? Do we entirely forget the significance of factors, the changes of which as well as their direct influence upon the organism often escape "exact" demonstration, it is true, owing to their apparent insignificance—*i. e.*, owing to the deficiency of the methods for their demonstration, but which attain an almost incalculable amount of influence in consequence of the continuous repetition of their action? If it is considered that an adult, to supply his body with the required oxygen, must have in one day about 110,000 pulse-beats and about 20,000 respirations, there can not be any doubt as to the increased amount of labor imposed upon the body by the slightest fluctuations of the atmospheric moisture and temperature.

But now one of the most important questions in the sense of the adherents of infection is not decided. Let me ask: Even if many persons in direct relations to each other fall sick, and if many inhabitants of one place or of one country become affected, is then *infection—i.e., the transmission* of the infection from one to the other—proved? If a shower of rain pours down and many persons are drenched at various places, may it then be said that one has been infected by the other with moisture? If of a great number of windmills one after the other moves more slowly and finally stands still, no infection will be held responsible, but we assume rather that the cause of the motion has now diminished its power or acts under unfavorable conditions. Any one who may believe that this example is too forced will kindly consider that the same principle holds good of electric currents, of abnormalities of pressure, and of the gaseous contents of the atmosphere, etc.

Altho cleanliness and neatness unquestionably are signs of higher culture, still it is absolutely wrong to believe that superlative cleanliness and neatness suffice to afford protection from diseases, and must, therefore, be striven for unrelentingly—*i.e., at the cost of other and more important purposes.* The fact that epidemics rage principally among that part of the population which does not comply with even the most moderate requirements of cleanliness and neatness—among individuals, therefore, who live in dirt, as it were—will always be adduced as proof of cleanliness. The observation is unquestionably correct, but the inference is absolutely wrong. These individuals will be seized by disease, not because they are uncleanly or untidy, but because, under the present conditions, cleanliness has become a virtue to be prac-

tised for its own sake, and only the weaker in the battle for existence have not the opportunity of practising this virtue. These individuals are not seized by epidemics because they are uncleanly, but because morally or socially they are on such a low level that they can not or will not apply themselves to cleanliness. The proof that uncleanness in the modern sense promotes disease, aside from skin diseases, would be adduced only if the conditions of life and of nutrition of the so-called lowest class of the population were rendered as favorable as possible long before the appearance of and during a disease, instead of, as is now done, enforcing external cleanliness and neatness of the dwellings only in times of an epidemic. Under such conditions, long before the appearance of an epidemic, after endeavors had been made to improve the conditions of nutrition of a class of the population without exerting any influence upon the cleanliness of their surroundings, if this class of the population would nevertheless be decimated, the conclusion might perhaps be permissible that cleanliness as such may be capable of preventing disease. Certainly with such an improvement of the social conditions it would soon be observed that the external dirt of the surroundings would then speedily be removed by the parties concerned, for every one who is fairly situated endeavors to adapt himself, so far as his means will permit, to the requirements made upon him by the improved condition of culture.

These remarks are by no means intended to preach the advantage of uncleanness; they purport merely to point emphatically to the fact that in our conclusions from the influence of cleanliness upon the percentages of cases of the disease and of mortality, and also in our en-

deavors for a practical proof of humanity, we are on a wrong ground, in that we pay more attention to the external appearance of matters than to their true nature. *Sanitary conditions are not improved by compulsion to external cleanliness, but the possibility of a better mode of life in itself is conducive to rendering man a cultured being who will then also practise cleanliness.* Just the modern theory of bacteria demonstrates, in the most paradoxical manner, that uncleanness is the greatest enemy of disease, because decay and decomposition arrest the development of the so-called special pathogenic agents. These pathogenic micro-organisms are at once destroyed if bacteria of putrefaction can develop, and hence they choose their abode in the living organism which, so long as it is alive, can not be the seat of putrefaction bacteria; the so-called pathogenic bacteria are the aristocrats among the micro-organisms. A filthy and foul-smelling drain is deservedly odious to the average man, but it does not furnish a favorable medium for the development of pathogenic organisms. If this were the case, then our villages would be constant breeding-places of epidemics, whereas experience teaches that just the cities, in spite of their endeavors for external cleanliness, are the chief localities of devastating epidemics. External cleanliness does not compensate for the want of light, air, and food, and is not a defense against the pernicious influences of certain trades.

The aim of hygiene can not be, therefore, to direct all the powers at its disposal at the combating of *one* pernicious element—always presupposed that it actually is the cause of an injury to the human organism; its aim must be *to determine the various influences impairing the function of the body, and the search for means of relief.*

Not the enemies with whom we measured swords after long periods of peace are the real terrible enemies, but the minute, yet constantly active, influences which slowly loosen the structure of the state and of the organism during peace, and which alone are instrumental in preventing a great action in the hour of danger.

Much as we are convinced that a furtherance of the true interests of hygiene and, with it, of its justified endeavors is in the very interest of mankind, as little can we reconcile ourselves to the views and aims which some modern hygienists (the "expounders of the law," they might be called) attempt to put in force. As little as we can regard the *threatening with heavenly and terrestrial punishment as the true hygiene of the soul or as the means of attaining cleanness of the soul in the highest ethical sense, as little can we agree that the health of the body is furthered solely by means of a theory of discouragement, by enumeration of the horrors threatening us, and of the punishment to be encountered by the sinner against the body.*

However, modern hygiene teaches preferably (the exceptions confirm the rule), so far as it looks upon bacteriological investigation as the chief aim of its endeavors: We are surrounded on all sides by enemies—the air, the water, the food, all harbor enemies ever ready to plunge upon us; our kindred, the friend who approaches us and offers his hand, may carry with him the germ of destruction; therefore, protect yourself against all touch, do not eat what nature offers you, do not drink what flows from its wells, do not breathe the pure, but only the disinfected, air; despise pure water as cleansing material, and utilize cauterizing, malodorous substances

to render your already sensitive skin still more so.¹ And, in order to justify such measures, we are shown how everything that surrounds us swarms with living organisms; people are made to believe that the mere presence of a foreign living organism signifies not only the *possibility* of an affection, but certain infection unless, with painstaking care, we destroy the organism. Man, therefore, is considered the defenseless prey of enemies surrounding him, whereas the history of the development of all organisms teaches that the point in question is not *a struggle of the organisms among themselves, but a struggle against the conditions of existence.*

The danger does not lie in the fact that an enemy is close at hand, for then we all were to perish; *but usually in that we, under conditions of existence unfavorable to us, furnish a medium for our enemies,* hence accord to them the conditions of existence which nature either withholds from us, or renders more difficult to us. *The microorganisms can not harm us so long as our organism functions normally; they are harmless if the defensive measures of our body are in good conditions.* We can not be

¹ Objection may be made here that the natural course of events in the realm of culture shows really that we always transform the pure gifts of nature according to our requirements before considering them fit to be used by us; however, this objection does not touch upon the true nature of the matter. We do not work up the products of nature only because they might endanger us in their original condition, but, above all, because a certain preparation and cooking enhance their value to us. We cook meat because in this form it is easier of digestion (at least, for the civilized stomach), because it keeps better, and because our taste is better gratified by the variety of preparation. To prohibit fresh fruit, milk, and water, or to allow it only when cooked, means to carry a theoretical principle to extremes, and to deprive us, for the sake of an absolutely unfounded and unproved theory, of material enjoyments and of healthy nourishment. To prohibit butter and cheese because cholera bacilli might vegetate in them is equivalent to destroying houses because rogues or criminals might lodge in them. Common sense can not protest with too great energy against such excesses of a false theory.

infected because the infective agent can not find a soil, as fire becomes extinguished if the fuel does not ignite. Hence the danger does not lie in the fact that we are surrounded by enemies, but in that an organism can not offer any or adequate resistance to prevent their colonization, so that they, as it were, live at the expense of the affected body—*i. e.*, of its labor (parasites).

This also applies to that series of cases in which infection actually exists. But such an infection is by no means present in every instance in which many persons are affected in a certain local or time relation; and even when micro-organisms are inseparably associated with certain manifestations—yes, are their cause, and even the cause of death—it still remains to be explained what constitutes the original weakness of the organism, the true *morbid disturbance* which enables any parasite to become dangerous—*i. e.*, to be transformed from a beggar that lives on the crumbs falling from the table into the master of the host. Every plum contains fungi and bacteria, but they are not dangerous so long as nothing is changed in the metabolism of the fruit. Not until after, for instance, abnormal dryness or moisture, frost, or an injury has become active and has altered the vital conditions of the tissues, will the enemies acting before the gate be capable of entering into the interior and of destroying it by countless multiplication.

What, then, do we accomplish by disinfective measures? Granted that an infectious substance—yes, even a living organism—is actually present (which, however, is relatively uncertain, according to our experience), granted even the seat and the quality of the infectious substance be known to us (which, unfortunately, is also rarely the case, since we generally pass off

suppositions for certainties), we must search for every individual focus of disease and must exterminate it separately, and that is, as shown by the example of greater epidemics (and of the *endemics of infectious diseases which are always present with us in spite of perpetual measures of disinfection*), an undertaking as troublesome as it is vain, quite apart from the fact that *external disinfection* will never be able to remove *germs of disease already present in the interior of the body*. What does it profit us to disinfect *externally* an apparently healthy individual who comes from a place infected by cholera, to bathe him, and to drench him with disinfectants, since by subsequent affection—immaterial whether it occurs hours or days after disinfection has taken place—he may furnish the strongest proof that our measures only choose the *surface* as a point of attack.

What we can do to protect ourselves is *to render our body so capable of defense that no enemy dare attack it*. The example of nations teaches that the best means to keep enemies at a distance is not war, the attack, but the development of our own strength (hence, of the capability of defense), which renders the prospects of an attack hopeless. If infectious disease really is a struggle between living organisms for the conditions of existence, the battle will always be decided in our favor if we are capable of strengthening our body so that it is unassailable, that it is able to retain the substances that are necessary to the preservation of the normal functions of the body so that no other living organisms are in a position to deprive it of them and to increase their transpositions in their own favor. Here, then, is the aim of true hygiene. It is essential that the conditions favoring the disease be investigated without preconceived

opinion and ascertained beyond all doubts without looking at them through the spectacles of a limited theory. We are still far removed from this point, since we may possibly in the main be acquainted with the conditions of life of man; but we do not know the most delicate influences, especially not the minute disturbances which in themselves do not signify anything, but the summation of which becomes very consequential in the course of time—*i.e.*, it reduces the working energy and the energy for resistance, and yet, in spite of apparently intact external capacity of function, renders the equilibrium so labile that then insignificant, otherwise ineffective, influences cause a marked disturbance of activity or even lead to collapse—influences which then are wrongly (*post hoc, ergo propter hoc*) considered to represent the (nearest) cause of the disease. Unnecessarily to explode powder when a single enemy exposes himself, or to fire blindly into space when an enemy is only *suspected*, does not insure any success, but only renders us excited and discouraged. If life is a struggle, then victory belongs to those that are calm and prudent, not to those who blindly rush forward; if life is a struggle, some must perish who are not armored as they should be. But victory in the struggle for life must finally come to him who strives not for the cheap glory of destroying the small number of enemies offered by somebody already diseased, but for a permanent peace in that he is unassailable.

Not the micro-organisms are the true enemy, but the unfavorable conditions of life, the *struggle* against the legitimate—*i.e.*, inexorably creating and destroying powers of nature. Be it our aim to shape this struggle so that we may be able to fight it under favorable conditions.

Since the machine represented by the organism can be kept in operation only in that the *amount of work performed furnishes as much energy as is consumed for the preservation of the connection of all parts*, the struggle for existence does not mean anything but to make the profit of labor as high as possible, and the expense of energy for external and internal activity as low as possible, in order to be able to employ the surplus again for a powerful stimulation of the labor of all parts.

One factor must be mentioned here which formerly played a great rôle, the significance of which at present, however, is underrated because it is a question of imponderables, or, let us rather say, of an agent that can not be demonstrated with microscope or scale. We mean the *will*. As the will often renders the weak strong, so can fear, the lack of will, the suggestion of a danger, so weaken the body that an existing disturbance in external nature becomes more powerful than would otherwise be the case. If we consider what influence is often exerted by one word, one sign of fear, upon the strongest, how, under the influence of a false, frightening representation in battle whole regiments suddenly turn uncontrollably to flight, how diseases spread among the disheartened and defeated, then we will not underrate the significance of fearlessness and of will-power also in epidemics.

The modern theory of the causes of infectious diseases has awakened hopes in two directions; one, pleasing to the representatives of science, that "the great unknown," the cause of disease, had in reality been found in the micro-organisms; the other one, invaluable to every friend of humanity, that the finding of the causes of diseases would also give the possibility of extermina-

ting these causes and the certainty to do away with diseases by preventive and curative measures.

Unfortunately, however, the conviction soon became manifest that a destruction of germs once colonized in the body by so-called germicides could not be accomplished in the manner as expected on the basis of the theory, and, therefore, the second problem was pursued with so much greater zeal—namely, the search for, and the destruction of, all germs, innocent and pathogenic, found within the body of man. But it appears that here, too, the premises are fallacious and that phantoms are being pursued; for an unbiased investigation teaches more and more that what was believed could be considered the cause of the disease is in many cases merely an unessential accompanying symptom, similarly as the advent of spring coincides with the coming of the birds of passage. The beginning of spring is not the cause of the arrival of the birds; their appearance is not always a sure sign that spring will really commence at once, but both events are in a certain chronological relation in a great number of instances. Only it must not be said that, if the birds should once happen not to appear on time, the season could for that reason not yet be spring, altho all other phenomena are characteristic of spring.

The mistake in such a contention is purely in the domain of logic, and it is often made because two or more events that are in chronological relation to each other are either erroneously brought into causal connection, or definitions are created quite arbitrarily in that a certain appearance is believed to be characterized by unessential attributes. For a child everything with a variegated collar is a soldier, every man with a beard a papa, whereas such collars and beards are not the essential

attributes of soldiers and papas; for there are soldiers with black collars and papas without beards, while persons with colored collars must not necessarily be soldiers and persons with beards not papas. These mistakes in the realm of logic were always at fault when arbitrary categories were created after apparently essential, but in reality unessential—because outer and accidental—characteristics, and this lack of logic is also the cause of our now declaring two absolutely identical cases of disease to be different because a bacillus is present in the one, and absent in the other, case.

Two strong persons succumb to a "disease" that resembles true cholera as one egg does the other, but because in one the bacillus developed in cultures—hence, under quite abnormal conditions of growth—and did not in the other, humanity, after a few days of anxious waiting and after both corpses have long since found a most rapid and unceremonious burial in palls drenched in corrosive sublimate, receives the comforting certainty that one of the deceased, because he had succumbed to "cholera nostras," could have been honored with the customary funeral without special disinfectory measures, whereas the other, even in death considered a danger to his fellow men, was justly deprived of all solemnities with which we honor our dead. How arbitrary this distinction chosen by bacteriology, and how little justified we are in taking decisive measures simply and solely upon this unsteady basis, is further shown by the fact that persons who are quite well—or, at most, show merely the slightest disturbance of their digestive apparatus—are registered as the most treacherous enemies of their environment because the dangerous bacillus has been found in conspicuously large quantities in cultures of their dejections.

Really, now that we know that such an extraordinary number of persons die of cholera nostras (*i.e.*, without bacilli), whereas others that harbor it in large quantities (or, more correctly, from whose discharges it can be cultivated in large quantities) recover—yes, do not even manifest any marked symptoms of disease—under these conditions, in which cause and effect are in such a decided contrast, should not the conviction at last become prevalent that the microbes in such a case can not be the cause of the disease, but that it is only a certain affection, or as yet unknown disturbances of function, that creates the nutritive conditions for micro-organisms? Should not at last the possibility be considered that an intestine that harbors so many microbes without harm may, under certain circumstances, even while the individual is perfectly well or suffers only from slight disturbances favoring the development of a certain species of bacilli, also offer an occasional opportunity to the growth in exceptional numbers of the comma bacillus or of any other form of micro-organisms?

Do we not behold in tuberculosis, in enteric fever, and in other diseases, that the number of so-called specific bacteria is often in no proportion whatever to the form and severity of the affection, to the functional disturbance, and to the final favorable or unfavorable termination? Likewise has it been shown in diphtheria that severe illness—yes, even death—may take place without the specific bacillus being present (so-called scarlatina-diphtheria), whereas actual pure cultures of the so-called specific pathogenic agent are observed in the mildest cases with scarcely noticeable membrane.

Nothing but uncertainty prevails wherever we look, and the microbe theory, far from making clear the cause

of the disease, only increases the number of ever-present interrogation points. *The bacillus as generator of disease*—as visible, hence apparently directly assailable, cause of the disease—has not, as many believe, acted as “consolation bacillus.” In fact, in our opinion, it has even *given rise to a most deplorable mental epidemic (namely, the bacillus fear)*, under the influence of which *the most important requirements of morals and ethics have unsubstantially volatilized. Humaneness and philanthropy have lately become foreign meanings, and those who scent the bacillus everywhere, and attribute to it mysterious power, are the cause of this deterioration and collapse of moral precepts.*

I can not resist the temptation of quoting in this connection some sentences from a pamphlet published by me some years ago,¹ to prove that the microbe doctrine in its outgrowth must necessarily lead to such consequences for our public life. They will show also to doubters that the doleful lack of judgment and humanity, the most deplorable expression of which was the treatment of the Hamburg fugitives, could not be surprising to those who endeavor to follow the development of the spirit of the age from its sources.

I then wrote: “We are, with our experiments to carry out practical disinfection, for the present restricted to the diseased body and its excretions, and we can not conceal from ourselves that the constant pointing out of this—in the eyes of many—*sole source of infection carries a very harmful effect in its train—namely, the fear of the patient*; for, under the influence of bacteriophobia, when formerly obscure causes of disease become *tangible* in the

¹ O. Rosenbach, “Grundlagen, Aufgaben und Grenzen der Therapie” [Foundations, Problems and Limits of Therapy], p. 115, etc. Vienna and Leipzig, 1891.

light of a new perception, we have forgotten that the *presence of microbes is by no means identical with the affection.*

“*The now-prevailing overestimation of the significance of microbes as causes of disease, therefore, is not only a sign of great ignorance regarding the relation between microbes and disease, but it also causes a further impairment of our knowledge, in that it closes to us the right road to investigation, the unbiased examination of the sources of infection. The very ones who appear to be predestined to observation and to collecting unobjectionable material—namely, physicians—are mostly not objective observers, since they are, as a matter of course, inclined to look for the source of infection where it must be searched for according to the prevailing theory of the moment. It appears as if, notably, water has always been regarded as the most convenient vehicle for the importation of the generators of the disease, or else general opinion in the middle ages could not have always so positively designated contamination of wells as the cause of epidemics.*

“*The greatest evil caused by the fear of bacteria is along social lines, or, as we would prefer to call it, along moral lines, since a goodly part of ethics is expressed in social relations. The fear of bacteria and of infection deteriorates our ethical views because it renders the relations of the diseased, possibly infectious, individual to his nearest environments as cheerless as possible. If a patient, because he harbors bacteria, is looked upon as the only and true source of infection, our own interests dictate to us to get as far away from him as possible, and to watch suspiciously over all his sayings and actions through which he comes in con-*

tact with us in the usual manner. The physician who sees how some patients and whole families are walled off and avoided because of the possibility of infection; those who, without prejudice, observe with what solicitude it is noted in the tuberculous "how he hawks and how he spits," not to learn by looking how he does it but to render him harmless; they will not understand why in this enlightened and humane nineteenth century we stigmatize the Spartans as cruel because they ejected their cripples, or the nations of the middle ages who exiled their lepers and permitted their pest-affected patients to die. How far are we even now from the time when the physician went to the pest patient with a black cloak and in a mask, with a vinegar sponge in front of his mouth? ¹ What is the patient to think if he beholds how even the physician is afraid to touch him, and how the latter, after unavoidable contact, acts as if by this contact alone the germs of disease had assuredly passed over to him? *Are we entirely unwilling to note the fact that physicians and the members of their families are not by any means more frequently affected by infectious diseases than other individuals who have nothing whatever to do with infectious maladies?*

"With such muddled conditions, with so little understanding of the nature of the processes proper, with such marked contrast between theoretical views and the facts of experience from which, with good intentions and without prejudice, the very opposite could and should be inferred of what to-day is regarded as the dogma as

¹ I call attention to the fact that the above remarks, and those that will immediately follow, are taken from an article published by me in 1891, hence do not represent retrospective prophesies, as are common in modern historical novels, in which kings of the Goths forebodingly predict the German Empire, or at least the North-German Confederation.

to the manner of the possibility of infection, endeavors are made to *encroach energetically upon social conditions* after it has been taught for nearly two thousand years *to love your neighbor and to care for the poor and the miserable*. Why extol the sacred bond of family and of society when attempts are made, with every so-called infectious disease, to loosen it, and pains are taken to transfer nursing of the sick to strange persons? I do not deny the value of certain disinfectory measures and do not plead against arrangements which owe their origin to the true insight into certain conditions, but, on the basis of many years of medical experience, I must regret most sincerely, like so many other physicians, that fear of bacteria which is nothing but the result of false scientific views, begins to manifest great disadvantages for human society. Apart from injurious social measures, quarantines, etc., resulting from an arbitrary handling of the veterinary police, allegedly in order to prevent epidemics of cattle, *it adds to the already existing social separation according to wealth the lasting separation of the healthy from the diseased, and it renders the lot of patients with infectious diseases—and which affection does not to-day, in the era of microbes, deserve the designation infectious—still more miserable than it naturally is*. Those that accuse me of exaggeration may compare the situation of the tuberculous in former years with that of to-day; let them compare the measures in scarlatina, diphtheria, and measles in former times, and those in the present decade! And if they can not agree with me, if they approve of our present over-activity which results from nothing but fear, let them furnish me *positive proof that the number of affections has decreased in consequence of our measures*. This proof might be difficult to be ad-

duced by him who utilizes entire periods and not merely the experiences of the most narrow horizon. The very fear of bacteria, the fear of infection, is perhaps most liable in times of epidemics to promote infection, for nothing is more harmful to the organism and its capacity for resistance than pale-faced fear."

In past days, when I maintained these views, I was met by the statement that the very knowledge of the causes also furnished the *means of easing the mind*; only an unknown enemy causes fear. I replied then—and I occupy the same standpoint to-day—that even in cases in which I could look upon microbes as the true cause I would not be able to value them as *consolation bacilli*, since my feelings of discomfort—like those of many others—were not during the war diminished by the fact that we knew the comrades who had fallen on our side were not made to bite the dust by a mysterious enemy, but by Frenchmen using bullets and shells. Only the conviction might serve me as a consolation that a *sure means could be derived from this knowledge of the causes* how to protect myself from these same bullets.

What do the efforts at disinfection, the allegedly efficacious means against microbes, accomplish? Disinfection is efficient only in those cases in which the disinfectant actually destroys the cause of the affection and, with it, the danger. There can be no doubt that disinfectants in strongest concentration kill living organisms. But it is doubtful whether the causative factor is always a living organism, and whether the mere exhalation of patients can be destroyed with such remedies, and whether the remedies actually reach the seat of the danger, since we are not able actually to disinfect internally, albeit this pious wish is cherished. But if the noxious

element is not a living organism, albuminous body, or poison in the ordinary sense, if a uniform disturbance of the vital conditions is the cause of the disease, then, even according to theory, measures of disinfection will be of no avail. And experience has confirmed this inefficacy in all those cases in which the conditions admitted of but one explanation.

Two tendencies are represented in the hygiene of today. The one seeks to destroy the pretended enemy with volleys of disinfecting remedies; everywhere in nature surrounding us it beholds the enemy and demands that our relations with the outer world are always subject to certain precautionary measures; hence it often startles us with false alarms, and then it naturally boasts of cheap victories until the enemy in great numbers surprises the fighter exhausted by continued attacks and by restless search and grasping after enemies that exist only in imagination, and makes him a ready prey (epidemics which, with insufficient conditions of existence for certain unfavorably situated classes of society, becoming in particular disseminated). The other tendency is that which endeavors to strengthen the fighter so that calmly and coolly, with a feeling of security that the attack will be repulsed, he expects the enemy. This, however, requires arrangements which, as we must frankly admit, are not in evidence as yet; for all the fighters in the struggle of life do not yet possess the chief weapons of defense: *nutrition, light, air, rest, and recreation*. These means of defense must, therefore, be created, difficult as it may seem to overcome old prejudices and to direct the interest of the well-to-do to matters the necessity of which is and has long since been fully appreciated by common sense, but which can be accomplished only by

active cooperation of all and not by a catchword, however high-sounding.

True hygiene must step in here. The hygiene of the future will not so much endeavor to destroy bacteria as to improve the vital necessities of man. Modern hygiene offers a stone in the place of bread, presents unproved dogmas and facts of the laboratory as substitutes for active aid and practical accomplishments. Intentionally or not, another and undesirable direction is given to the reasonable endeavors and rational requirements of hygiene. Under the device, "Disinfection and extermination of germs," a mere catchword is substituted for the genuine values with which true hygiene must reckon and must attain the end of improving human existence.

Not catchwords and small means can help, but the remedies of old renown: Light, air, plenty and nourishing food, and rational alteration between work and rest.

We are satisfied with gratifying the requirements of the laboratory science called bacteriology, and endeavors are made, under this catchword, to enthrone the fashionable scientific idol in place of the ideal, the humane and ethically valid conception of "hygiene." Because we do not see or do not wish to see where the lever of improvement must be applied, or because we believe to improve the lot of mankind with the one-sided furtherance of bacteriological aims, the noble endeavors of hygiene are confounded with the limited requirements of the microbe theory, and the struggle against bacteria is called "hygienic aims." The aims are confused, and the means and time, labor and money are wasted upon an effort which can not be of advantage, since it intends to influence from petty view-points the rule of natural laws

which obtain in the struggle for existence, not hidden to those that are able to see.

Disinfection is to hygiene as is the strict observance of certain outer forms and precepts to fulfil the *substance of the laws of morals*. Fasting and mortification are not signs of morals, but practical carrying out of ethical precepts, resulting from the recognition of their *necessity* to the preservation and elevation of mankind. We appear painstakingly cleanly in that we clean the surface of things symbolically, but, unfortunately, we neglect the real internal cleansing—*i.e.*, the true strengthening of body and mind. If, in times of an epidemic, instead of giving directions what to eat and what not to eat, care would be had, instead, that those who have nothing to eat are supplied with sufficient food; if, instead of poisoning the air with carbolic acid and other disinfectants, the money were applied to other purposes, and pains be taken to see that those whose dwellings are small have an opportunity of getting plenty of fresh air and as often as possible; if, finally, by instruction, not by authoritative compulsion, endeavors were made to disseminate the knowledge of the true relation of events, and to explain the deception of many views which infuse fear or lead to wrong actions, then true hygiene would be promoted in the same manner as the health and the well-being of man is furthered, not by promising to furnish medicine when he falls sick, but in that he is prevailed upon to live so that he does not become subject to disease. But to promote a mode of living agreeable to nature does not mean, as many believe, to proclaim a number of directions as to what is permitted and what is prohibited; for, apart from the fact that many of such directions are not sufficiently well founded and owe their

existence merely to prejudice, apart from the fact that our food, taken moderately, can never do harm, the prohibition of certain food for certain classes of the population is to no purpose whatever, since the difficulty of the conditions of existence in this case does not permit of any choice, but the *compulsion* of circumstances dictates the variety and the quantity of the food. Dietary directions are a luxury, usually unnecessary, which only the upper ten thousand can afford. *To live naturally means so to live that the care for the existence is eliminated, that the vocation does not exhaust mind and body, that the food is in accordance to the taste and requirements of the individual, that the dwelling is pleasant and airy, that sufficient sleep is had, and that time for recreation is not wanting.*

Hence the watchword for the future must be:

Not fear of bacteria and measures of disinfection, but improvement of the vital conditions and development of independent thought and action in accordance with the requirements of social ethics.

XIX

SIGNIFICANCE OF SEASICKNESS WITH REFERENCE TO THE THEORY OF INFECTION AND IMMUNITY

SEASICKNESS is the typical picture of an epidemic (*mass*) disease; for many individuals under the same conditions of life are affected in a connection that, without knowledge of the real etiological factor and only on the basis of the superficial—but very common in the explanation of mass diseases—method of inference *post hoc*, we are absolutely forced to assume an intoxication from the gastro-intestinal tract or an infectious element—*i. e.*, we are bound to determine an auto-intoxication, a poisoning by food; in short, an *endemic* or *epidemic*. If we consider the succession of the cases of disease: those affected first are the weak persons that stay below deck, especially women, then men, whereas nurslings, who take different food, as is well known, are usually exempt; if we consider further that close contact with a patient favors the outbreak of the disease—perceptions made by eyes, ears, and nose, hence the proximity of the patient, unquestionably increase the predisposition—then it would by no means be difficult to construe here a disease by *infection* and to regard as the center of the infection, perhaps, the lady who was the first to be affected in the presence of the public, in the *salon* or on deck—of course, always assuming that we do not know or that we wish to misjudge the true cause of the affection. As a matter of

fact, an outbreak of cholera on shipboard may probably take place under very similar conditions; at any rate, a person fully immune to seasickness and ignorant of the conditions, who would observe one after the other of his neighbors at the table leave the dining-room, looking deathly pale, could not help believing that an infection or poisoning be present.

Therefore, seasickness demonstrates to us that a *simultaneous occurrence* of homogeneous and severe cases of disease does not constitute a *dependence* of the different cases *upon one another*—*i.e.*, a transmission—any more than the conclusion is permissible, from the fact that persons surprised by a heavy rain are drenched, that these persons had transmitted the moisture from one to the other, or, in case they acquire a cold, that they have infected each other.

Epidemics, or pestilences, are by no means always transmitted from case to case or possess a center of infection. A starting-point (for our observation) and a center of infection are not always identical; for every series of events must have a first one, but not necessarily a connection. The difference between an *epidemic disease* (*pestilence*) and the *endemic of seasickness*, which may attack many hundreds in a few hours, consists only in that here we know the cause, whereas in the former case it is unknown, and is usually replaced by a more or less obvious hypothetical one. Only because we are not familiar, or misjudge, in epidemics the homogeneous but not always equally powerful influences upon agencies which affect all individuals alike—perhaps the alterations of the external currents of energy, of the life conditions; in short, of the conditions under which the machine of the organism performs its work of

transformation and preserves its tensions—merely because these *fluctuations of the energy currents* forming the basis of the disturbances are not as comprehensible to us as is the rocking of a ship at sea and the connection of these alterations of the conditions of life with seasickness, do we feel called upon to set up hypotheses changing with the fashion regarding the mechanism and the causes of epidemics, and, following the simplest ideas, we almost always accuse the digestive canal as the portal of entrance for all noxæ, as tho the organism were connected with the outside world only through the mouth, and could be injured merely by visible and ponderable noxæ and not also by energy currents, the transformers of which are the external skin and the mucous membrane of the air passages.

Seasickness proves that physical disturbances (in the widest sense) are able to act at least as energetically as the tangible or hypothetical chemical ones, that they also may sometimes be the main cause of disturbances which the representatives of modern science (who, as is well known, deny also the "refrigeration," the effect of the cooling of the skin or of the nerves upon metabolism) attribute preferably to smallest *living organisms* or *chemical poisons*. Again chemiatry (and the theory of exclusively chemical irritants) plays the dominating part in our science, whereas history and simple reflection teach that physiatry and chemiatry, solidarity pathology, humoral pathology, and neuro-pathology represent but *limited* views of a part on the *gigantic structure* which, as *metabolism*, comprises the recognition of all forms and disturbances of the workings of the organism.

Seasickness unquestionably teaches that severe affections of the gastro-intestinal tract and of other organs are

caused solely by physical influences—*i.e.*, by certain impulses affecting the entire body, and thus many an adherent of the modern theory of infectious diseases might be induced to ponder whether or not disturbances of the gastro-intestinal tract of certain individuals in Asiatic cholera and cholera nostras may not be merely signs of an altered activity of the respective tissues which, under certain external conditions—perhaps in case of excessive demands upon the transformation activity of the skin or of the hematopoietic organs (by heat, etc.)—are called upon to fulfil demands which they are the less able to comply with if the blood or the skin supply them with insufficient energy (currents of deficient kinetic value). But if once the possibility of the occurrence of a considerable intestinal insufficiency (for essential, internal, and for extra-bodily labor) is present upon this basis, then it is demonstrated, for instance, that the comma bacillus is not the true cause, but a secondary manifestation, an *accident*, of the affection, a nosoparasite, according to the excellent designation of Liebreich; that, further, the disease is not always infectious, and *that even a pandemic must not be traced exclusively to an infection or poisoning*. At any rate, to secure the relationship of the individual cases by the connecting link of transmission requires still other proofs than those which heretofore were considered sufficient. Indeed, the frequent fatal terminations in cholera nostras show strikingly that disturbances of metabolism alone—*i.e.*, even without the bacillus (proclaimed by Koch to be typical), are sufficient to bring about the fatal result by the same disturbance of metabolism.

Seasickness further shows conclusively that the manifestations of the disease do actually disappear with the removal of the cause, but only when no changes of essen-

tial, internal (tonic) labor have as yet taken place, when the regulation for pathologically intensified reaction has not occurred yet—*i.e.*, the more marked displacement toward the direction opposite to the effect of the irritation. Let it be remembered that, in almost all cases after the cessation of abnormal irritations—immaterial whether they have primarily caused an irritation, hence a special quantity of relaxation of energy, or an inhibition, hence especially marked tension of energy, in the organism—the *opposite form of equilibrium* must take place, if it has not in part existed even during the action of the irritation. For instance, if abnormal irritation is followed by an abnormal tension or exhaustion as secondary symptom—*i.e.*, by non-irritability—this new far-reaching displacement of the average equilibrium may in itself also be a cause of conspicuous manifestations of disease which, however, are fundamentally different from those of the first stage—etiologically and also in particular with reference to therapy to be adopted. This can be noted especially in seasickness. If the affection has been particularly intense, or if the disturbance has been of longer duration, then more or less well-developed symptoms of vertigo will remain for several days after landing. This *after-vertigo* indicates that the organism which by this time had gradually adapted itself to a new form of utilization of the equilibrium, still continues to give on *terra firma* the impulses of innervation in the direction of the first abnormal utilization—*i.e.*, in such a manner as tho it were still compelled to compensate the abnormal movements of the ship. This is the reason why the disturbances occur not so much during more marked movements, hence upon more pronounced innervation which hypercompensates the perverse regulating

actions, as during the transition from motion to rest in the horizontal position ; yes, the unsteadiness appears sometimes to be as pronounced as in the cabin of a heavily rocking ship. The after-effects are especially intensified during the position of rest, because on shipboard the habit had been formed to regulate especially for this position, and because the abnormally marked regulatory irritations in convalescents from seasickness in the position of rest are not diminished in proportion to the others, hence upon cessation of the impulse for normal erect carriage. Since they served in particular for compensation of maximal irritations, they continue to act, altho less intensely, and most markedly displace the average equilibrium in the horizontal position. Therefore, the cure (by adaptation) in after-vertigo is best brought about in that impulses similar to those as otherwise produced by a slightly rocking ship are given by the affected person himself (*i.e.*, recovery will take place the sooner the less the patient is induced by the phenomena to persist in keeping the horizontal position), hence the more impulses are given for marked motions, endeavoring to overcome the abnormal innervation of regulation by external irritations in the sense of a displacement from the normal equilibrium. (This rule applies also to the cure of other forms of vertigo in nervous persons in whom relief can be procured only by energetic motion which, it is true, is at the beginning dreaded by the patient.)

These cases teach, therefore, that in secondary manifestations of the disease which, like after-vertigo, already represent a change in the direction of regulation, hence the form of displacement opposite to (primary) reaction, the simple endeavors to remove the (first) cause are no

longer sufficient to dispose of the disturbances, and that the remedies in these instances must be different from those employed in cases in which the point in question is merely the combat against the primary reaction (action). It follows that *the battling merely against the presumptive or true cause can not under all circumstances be the correct road to cure*, especially not after the acute stage (action or first reaction) has run its course.

If secondary symptoms are present, resulting from compensatory efforts, the introduction of the most efficacious counter-irritants—yes, even of direct antidotes (to the first irritation), if we actually are possessed of such—would not be conducive to cure, but only once more most markedly affect the already active energetic of the organism. In other words, an antidote derived from the theory of the irritation (specific remedy) is, apart from other circumstances, only then indicated and rational when it may be presumed that the original irritation is still active; that, therefore, all existing symptoms (or, at least, the most important ones) are *the expressions of the action of the irritation* and not as yet that of *regulation*. If this important fact is not taken into consideration, the remedy must act the more injuriously the more marked efforts at regulation are manifested by the symptoms under which it is employed.

Thus we have arrived at a point of great importance—namely, the investigation of the question of the *significance of seasickness with reference to the theory of immunity*. If it be considered that nothing protects better from the disease than *habituation* to the motions of the ship, and that the majority, even after a relatively brief duration of the disease, remain free from it for the rest of a long voyage, then it is beyond question that immunity

belongs to the category of processes or conditions which we designate as *adaptation*, respectively *practise*, to which fact we have called attention some time ago. We become accustomed to the abnormal irritations which the rocking of the ship represents for the energetic of warm-blooded beings, as persons living continually in the open air become used to the changes of the weather and to the fluctuations of the temperature, the laborer to the weight of the burden, the mountain climber to the irritations caused by mountain disease.

The method and the purpose of *immunizing* should not principally differ from the process and purposes of *adaptation*. The former should aimfully imitate the mechanism of adaptation—hence, artificially employ the factors (irritations) which probably will be capable of creating a new form of activity, presumably quite necessary for the future, but which, under ordinary conditions (during normal activity) probably can not be formed. Every form of immunization, therefore, presupposes the application of correct irritations, which must be based upon the perfect knowledge of demands arising later on, and, above all, the possibility of a formation of varieties and quantities of energy (latent reserve energy) intended to act as a correspondingly higher counterbalance to the expected abnormal effects.

Artificial immunization, therefore, should develop, as it were, a dormant predisposition by foreign, exogenous irritations equally methodical, as is done by *practise* through definite impulses of the will (hence, by internal irritations), or, as nature achieves it, by slowest (regulatory, systematic) raising of irritations and productions with sufficient supply of energy (development). Immunization is to effect for somatic metabolism what natural

development accomplishes by shaping the predisposition in the given (appropriate) direction, by rational education—*i.e.*, by appropriately graduated artificial effects; namely, to utilize the existing reactive and regulatory contrivances in a correct proportion and to supply stores of tense energy by uniformly increased activity for the expected form of utilization.

The problems and limits of therapeutic immunization can be clearly derived from these considerations. *An acute and at the same time lasting immunization is a contradictio in adjecto*; for the large amounts of energy permanently at hand and necessary to accomplish it can not be obtained by means of mere effects of irritations which, after all, can serve only as libration of existing ready or potential energy, but do not in themselves represent corresponding quota of labor energy for mass displacement and tension. The formation of the latter naturally requires productive material and the corresponding time. If, then, immunization is equivalent to adaptation, if adaptation represents a series of development rising from minimal changes to a maximum,—hence, to use the technical term, a chronic process (characterized by the summation of minimal quantities)—then acute immunization is a logical contradiction, like, perhaps, acute practise or acute education. An immune body can owe this quality only to a *primary characteristic* (hereditary predisposition), or to an *adaptation* that had already been active, which, however, always requires time.

That a (relative) *acute development* exists is beyond doubt, but only a *dialectic* difference is present in this definition in that acute development presumes that all forms of energy, all forms of tension, are already so perfected (or given con-

structively) that the chain of processes can move with corresponding rapidity if corresponding irritations are active and nothing disturbs the course of events. If, therefore, a development in a certain direction is to be accomplished acutely, it is imperative to be sure that the object of development is in a proper condition—*i.e.*, possesses the required great energies of tension and activity; for, if the energies of the body do not offer sufficient counterbalance, the *maximal* (artificial, one-sidedly acting) *irritations* (processes of causation), after consumption of the energy on hand, must become the cause of abnormal displacements which, according to their duration and extent—*i.e.*, to their significance with reference to the extra-bodily or essential (internal) labor, must be considered *changes of function* or even *disease*.

The preservation of the *vital*—labile and yet stabile (dynamic)—*equilibrium* of the tensions in the body, the preservation of health and capacity for action, in spite of considerable one-sided increase of function by enhancement of certain stimulants, is only possible, therefore, if continually large quota of energy of opposite forms are on hand. Naturally, however, these conditions are not always complied with in many cases, and this constitutes a great danger; or, in other words, *every efficacious acute immunization must signify a danger to the metabolism*, to the preservation of the condition of equilibrium of the organism which prevailed heretofore.

If a considerable increase of activity is to be achieved more rapidly than in the natural way, the body is exposed to the dangers of a *crisis* or catastrophe, in that, relying upon auto-regulation, we expect it to perform an amount of labor which by far surpasses the usual productions; for the organism utilizes only *minimal* irritations—namely, at once to consume its material of energy of a certain form completely or in considerably larger amounts than ordinarily, and still maintain the former

equilibrium. As surely as it may be expected that a certain irritant, incorporated in sufficient quantities, produces an acute disease (maximal alteration of the extra-bodily labor, owing to a change of the labor performed for essential, internal, activity, caused by the shifting of the balance of energy), quite as surely will the proper counter-irritant produce the opposite form of disturbance. This injurious effect fails to become manifest only when a relatively insignificant quantity of the irritants allows sufficient time for a gradual increase of the chain of librations (hence, to intensify the productions only in the course of time), as is done, for instance, in regular muscular practise; then, indeed, success regarding paralyzing the effect of abnormal influences can surely be accomplished.

These propositions apply to *all forms of the irritations*, whether they represent conscious (of the purpose) acts of the will for the accomplishment of certain (often appropriate) forms of motion (practise), or whether they act only by reflex (adaptation). It follows that all encroachments upon metabolism are borne with greater difficulty, the greater and more lasting are the abnormal irritations, the less perfect from the very beginning is the equilibrium or the capacity for its regulation, and the smaller the quota of energy (stores of latent reserve energy) which form it; for alone upon the possibility of complete compensation of the shiftings produced by the irritations depends, after all, the possibility of the preservation of the functions existing so far intimately connected with the definite average equilibrium. As easy, therefore, as is gradual adaptation, as difficult must be the acute form.

Acute adaptation, or, more correctly, a complete and

lasting compensation of irritations by a stock on hand of energy answering even maximal requirements, can *a priori* be possible only in a minimum of the cases—namely, when it is a question of impulses that are not too powerful, or of processes of liberation of not too long duration. Such a compensation is not at all possible in a great many cases, even for the shortest period of time; for the *quantity of energy on hand in the organism is limited, whereas the quantity of external impulses is unrestricted.* Therefore, the majority of cases will suffer, even upon a slight increase of the irritations, a more or less lasting disturbance of the extra-bodily function—for the preservation of the visible (average) activity—until the energy quota for the establishment of a new equilibrium—corresponding to the new irritation—are supplied by the intensity of the internal labor.

The difficulty for acute artificial adaptation is due, therefore, to the fact that it is so very difficult to imitate the natural process, because *nature*, in cases in which *sure* results are obtained, works with *smallest irritations* and in *long periods of time*; because in all cases in which changes take place without regard to the medium (to its bodily individuality)—in which, therefore, only the final result of development is to be considered (not the manner of transformation, of the shifting of the equilibrium of the medium)—a *catastrophe* occurs which endangers the individual existence of the medium. These catastrophes in the organism are the acute diseases which certainly produce for the majority (*i.e.*, for those that recover) a sufficient result of immunization, a certain faculty to overcome certain requirements—to be sure, at the risk of destruction of the individual existence.

Thus we may not hope to combat the outbreak of sea-

sickness more potently than by *slow adaptation* to similar irritations, or, as is usually the case, by adaptation to the motions of the ship, which then, for a certain length of time, brings immunity to the majority.

However, what holds good for seasickness applies also to all other forms of changes of metabolism due to abnormal irritations which we call, so long as it is a question of an influence upon extra-bodily productions, functional disturbances, or diseases when the point in question is an influence upon the essential (parenchymatous) labor. The influence upon metabolism is the same, in potent irritations and with the proper time of action, whether the source of the abnormal kinetic impulses is always situated outside of the body (exosomatic irritation) and the current of centripetal undulations enters the body only by transformations (*genius morbi* in the widest sense—*i.e.*, physical and chemical effects of the external media), or whether the abnormal influence manifests itself to the mechanism in form of microbes or toxins—hence, of masses which become active only from the interior of the body. The difference is only that the person with seasickness is sure to be free from the disease after a certain number of days, since the irritation becomes extinct on land, whereas the organism which suffers by an accumulation of abnormal irritations in the interior of the body is usually confined to its own regenerative power—*i.e.*, to the capacity of destroying the noxious element directly, or at least to render it harmless by new forms and quantities of internal tension, because only in rare cases may we count upon the spontaneous extinction of the noxa.

Thus, as little as a person not immune to seasickness may be really made immune to the disease (respectively

to the effects of the rocking of the ship) by the most violent movements of the latter, to which he exposes himself only for a brief period of time, as little is it possible to confer a permanent protection from all, or only a temporary protection from intense irritations of a certain form by *acute immunization*—*i. e.*, by *prophylactic inoculation*, tending to render the body invulnerable to infection in the briefest period of time. Such a hope is quite as Utopian as that of protection from seasickness by the prophylactic administration of a narcotic, or by the incorporation of a serum taken from a person immune to seasickness.

The objection that the irritation of inoculation continues to operate as the generator of waves in the organism, whereas (in the above-quoted example) the movements of the ship that had been effective for only a brief period of time, had not been active sufficiently long, is not very demonstrative, since experience teaches that tuberculin very rapidly becomes ineffective, and that also the curative serum for a short time only calls forth those manifestations with which protection is claimed to be connected. Therefore, the above-mentioned inoculation remedies are not as efficacious a protection in this sense as is (smallpox) vaccine, which has in its favor at least that it displays in the organism an insidious (chronic or subacute) action as yet not achieved by other means—hence, tends to accomplish a process which in a certain respect is more analogous to normal adaptation. Nevertheless, even the duration and the efficacy of protection accomplished by the last-named process appears to be so problematical that the circumstances concerning vaccination and protection by vaccination must constantly be submitted to renewed critical reviews.

The observation of diseases such as seasickness affords special opportunity again and again to point out that the object of medical endeavors *can not be the therapy of fully developed disease*, the careful protection from all influences from without, or *planless disinfection*, but only hygiene—*i.e.*, the recognition, creation, and utilization of appropriate conditions of life. The physician of the future will be compelled to consider, above all, prophylaxis, the rational distribution of the productions for internal and external activities—*i.e.*, the correct *alternation of rest and labor*, the appropriate *adaptation to changes of the external conditions of life*, and the practise, the harmonious development of all physical and mental functions. He will not, in the frame of a formal diagnostic systematism, as a cellular pathologist grasp after symptoms pathognomonic of local changes of tissue, but he will endeavor, as a *biologist*, to obtain an extensive view of the *the realm of energetics* (the province of which is modern organic physiology) and of the total *balance of phrenosomatic activity*. This activity, after all, is productive (for the preservation of the individual) only in thorough harmony between internal (tissue) and external (organ) productions, and the extent of a visible function is often as little a proof of health and productive capacity as the brisk and noisy activity of the machines in industrial concerns is a sure sign of the prosperity of the enterprise.

XX

IN HOW FAR HAS BACTERIOLOGY ADVANCED DIAGNOSIS AND CLEARED UP ETIOLOGY?

IF diagnosis is the art of inferring from a number of visible and otherwise demonstrable changes of the general condition or of single organs the most minute alterations in the economy of the body, which endanger the continuance of individual elements (energetes, cells, tissues, organs), and finally the continuance of the entire organism, we do not require the means of diagnosis to arrange the disturbances of energetic determined in such a manner into a nosological system, but to cure them or to prevent them.

Diagnosis certainly is also intended to enable us to formulate a prognosis which is of importance for the social conditions, but its great significance consists in the fact that it furnishes the possibility, by appropriate and well-timed (hygienic, respectively prophylactic and therapeutic) actions—in the direction in which danger threatens to the ingenious dynamic equilibrium of the activity of the organism—of preventing disturbances entirely, or of accomplishing the restoration of the average equilibrium (tonus) after a number of necessary fluctuations and undulations which must represent processes of regulation not merely processes of reaction.

In order, therefore, to determine the progress in the realm of medicine (and in the medico-scientific domain)

produced by new, especially bacteriologic, view-points, it is essential to establish at first whether and to what extent the above-named postulates have been considered, whether we are dealing with a mere change of the systematic observation, with a re-creation of scholastic definitions which simulate positive acquisitions only by an altered grouping of facts, by a change of perspective, as it were, or whether the reform of methods (of the means of thought and recognition) is actually instrumental in bringing about the mastery of conditions, an advantage for the welfare of sick humanity.

The starting-point in this investigation will be the domain of *diphtheria*, because, according to the judgment of those concerned, the advantages of modern diagnostics are most tangibly prominent in this particular affection. Yes, the adherents of orotherapy even proclaim the early bacteriological diagnosis of diphtheria to be, as it were, an infallible means, respectively the *conditio sine qua non*, for a certain cure of the affected, and the safest basis of protection for those threatened with infection. The demonstration of specific bacilli at once furnishes the recognition of the nature of the disease; only those that are infected by specific bacilli are objects of cure, and with certainty at that, if they are subjected to treatment on the first day of the disease. The weapon which caused the wound furnishes the only means of cure; hence, it is of importance to ascertain the nature of the enemy as early as possible.

How, then, is it to-day with the diagnosis of diphtheria? The diagnosis is claimed to be rendered absolutely certain and easy by means of the bacteriological method, because a minute determination of the pathological picture of the difficult examination of the organs of the

throat is no longer required; all that is necessary is to take a small quantity of mucus from the mouth and to make a simple culture experiment in order to furnish the exact proof as to the nature of the disease, perhaps in the same manner as the presence of sodium is determined by the spectroscope. Granted, then, that this proof actually is rapid, easy, and positive, since the characteristics of the diphtheria bacillus are especially distinct, and hence the results of cultures less subject to objection than those obtained from the inspection of the diphtheritic membrane at the seat of the affection, *i.e.*, in the throat of the patient, and from the careful examination of the other conditions; granted, even, that an experienced physician would be longer in doubt regarding the condition of the patient—purposely we do not say regarding the diagnosis—than a bacteriologist regarding the classification of a bacillus, what has been gained for medical and human purposes? It is impossible that any form of systematism should be the aim of our efforts, since the point in question is not to give to a disease a name, but to judge the possibilities of recovery, to remove the dangers to the patient and his surroundings, and to find the means for recovery. What, then, is gained by determining the microbes? Scarcely any more than by the spectroscopical establishment that sodium really exists everywhere; for, as little as the presence of most minimal quantities of this substance will induce us to regard all apparatus as soiled and all analyses as abnormal, quite as little will we obtain a hold for our medical actions by the presence of so-called diphtheria bacilli, especially if they occur in small quantities and were obtained from a flake of membrane.

The development of a certain culture from a specimen

does not by any means permit of a sure, unqualified inference as to the conditions in the organism ; it is little determining of the assumption that the microbes obtained in this manner are the only ones present in the organism, that they are under equal conditions of development, or even are the cause of the disease. . . . In order to draw unobjectionable conclusions, it would be necessary to obtain in every case a number of specimens from different regions, from healthy and affected parts, and the results of numerous microscopic examinations of the contents of the mouth should be compared with those of numerous bacteriological investigations upon different media, quite apart from the fact that the parasites obtained from the easily detachable membrane are not identical with those that are present in the tissues—*i.e.*, as little represent the real pathogenic agent as the insects enclosed in a piece of amber are the cause of the origin of the amber.

Is the danger for a patient with the bacillus greater than for one who is without it? Certainly not ; for the cases of so-called scarlatinal diphtheria, in which the characteristic bacillus is entirely absent or is covered by proliferations of other microbes, are especially dangerous. Besides, there are plenty of healthy individuals who have the bacillus and remain healthy, just as, fortunately, the majority of the patients recover easily and rapidly despite the bacillus. Neither is there any reason to believe that such carriers of the bacillus endanger their environments more than those who have no bacillus ; furthermore, scarlatinal diphtheria is at least quite as much or quite as little infectious as true diphtheria, altho in the former case microbes (streptococci or staphylococci) are determining (*i.e.*, dominate the scene for the bacteriol-

ogist) which otherwise are present everywhere—hence, represent normal parasites, as it were, of the cavity of mouth, respectively of the skin.

Let no objection be made, therefore, that the diagnosis of diphtheria has now become more certain by the demand and the possibility of demonstrating the "specific" ¹ bacillus, quite apart from the fact that the determination can not be accomplished as simply and rapidly as is generally believed, since, first, a negative result of the bacteriological examination is not a proof of the absence of the bacillus, which frequently does not develop sufficiently or characteristically until after twenty hours (therefore, it takes at least twenty-four hours before a decision can be had), and, secondly, if the development fails to take place, the objection is not yet refuted that specimens of membrane taken from other parts might have given a positive result. To this is added that the perfection of the media—*i.e.*, their special fitness for a certain micro-organism—obscures the state of affairs, since such media impair the development of other, possibly more important, forms, or they favor the development of one species at the cost of the others.

Therefore, the assertion of the uncertainty of the former criteria and of the infallibility of the new form of diagnosis is one of the fallacies always employed by the scientific or unscientific apostles of a method in order to influence public opinion in their favor. But even suppose—altho it is not admitted—that the fundamentals of diagnosis, altho not more reliable, still have become more

¹ We may now with satisfaction point to the fact that since the publication of this article the specificity of the Löffler bacilli has been disputed by many other investigators, among others also in the publication written under the direction of Baumgarten.

uniform than formerly, this is not an acknowledgment that formerly we diagnosticated differently, utilized different material, than we do now, and that for this reason the former and the present figures must not be compared, or are comparable only when the old principles of diagnosis would again be employed.

Would any physician of the former period have dared to designate cases as diphtheria in which the throat was sound and the general condition undisturbed? And yet this is done to-day. Was it perhaps customary formerly to differentiate strictly between scarlatinal diphtheria and diphtheria proper, and thereby to reduce the mortality statistics of so-called true diphtheria by a considerable percentage? Let it not be objected that formerly the deaths from scarlatinal diphtheria were added to the mortality group of scarlet fever; for that applies only to a small number of cases in which the affection of the skin could be determined with certainty, but not to the many cases in which the cutaneous eruption was absent. Was it customary formerly to place mild cases which possibly presented only one of the many throat phenomena at once in the category of diphtheria? Were not many cases, just on account of the mild course, in spite of doubts entertained at first, rather looked upon as simple inflammation of the throat, if for no other reason but not to be suspected of exaggeration and to alarm the patient and his relatives needlessly? Now, however, it is dared to determine the disease with certainty on the first day—*i. e.*, at once to render an important decision regarding the danger to the patient and his environment; it is true, the power is also claimed to be able at once to reduce the danger to naught, since the infallible remedy is at hand.

It can not even be admitted, therefore, that the certainty of a diagnosis has gained by the application of the new view-points or methods; only the certainty has been increased to recognize one distinct sign more positively than formerly—*i.e.*, the presence of a bacillus of allegedly special properties can be determined after the lapse of less time than was formerly the case. It corresponds about to the advantage offered to the superficial observer by the methods of thermometry, which certainly, in the hands of a careful physician, also admit of a frequently warranted conclusion regarding the duration and the course of the disease, altho I do not at all intend to identify the importance of this method with the mere determination of the presence of the bacillus of diphtheria in a particle of membrane of the mucous membrane, since this fact, in our opinion, does not furnish any support for abnormal processes in the organism, let alone for prognosis and therapy.

According to the nosological importance, we must differentiate:

- (1) *Accidental* micro-organisms, true (benign) parasites, ectosites, surface parasites.
- (2) *Histosites (endosites)*, which are again divided into
 - (a) *Nosoparasites* (according to the designation of Liebreich)—*i.e.*, into the class of secondary noxæ, and
 - (b) The directly *pathogenic* organisms, the class of primary noxæ.

Before it is permissible, therefore, to express an opinion concerning the importance of microbes for the metabolia, to represent them as generator or signs of disease, the determination is required in every case whether the development of a certain form of bacteria is only an unes-

sential accompanying symptom, whether it is in any coordinate (symptomatic), or already in an essential (causal) relation to the disease. In this determination it is a question of the second part of every scientific investigation, of the logical (deductive) utilization of the facts obtained inductively.

To demonstrate this by as drastic an example as possible: The advent of the birds of passage coincides with the appearance of spring; but to conclude from their arrival that spring was really at hand, or that there could be no spring without the appearance of the birds, is wrong. The arrival or presence of the birds is an accidental factor, since the birds of passage may at one time fail to appear or arrive at another time much too early. The growing heat of the sun is possibly or probably the cause, certainly one of the most important signs, of the change which we designate as spring; that the plants growing in the open air become verdant is also an important sign, inasmuch as the chlorophyll could not develop without the alterations which occur in the train of the change of the climatic conditions; but this is not the cause of the change. The arrival of the birds, therefore, is of less importance to the diagnosis of spring than that the plants in the open air become verdant; both phenomena are in a certain, but different, relation to the change in the conditions upon the surface of the earth. The former is an equal, coordinate, accidental factor, the second a subordinate (consecutive) one. The heat of the sun is scarcely in an etiological relation to the first, but surely to the second, phenomenon—*i.e.*, the instinct of the birds to migrate can not possibly be due to the fact that the temperature becomes higher in a locality many hundreds of miles away from their abode; but the impulse to fly north usually becomes manifest at about the last-named moment. But that the plants become verdant in the open air indispensably requires sunlight, possibly also the heat of the sun. In how far this latter is the general cause of the change which we call spring, we are not able to judge; but it is certainly an important factor, after all.

Similar considerations apply to any form of experimental demonstration in the realm of biology, since it can, under the existing conditions, assume only analogous instances at best, but never homologous or even identical ones. The experiment holds good only for a given case; it does not admit of a far-reaching (analogical) conclusion. The belief that the same directions and tensions (norms) of energy must be active in general conditions and everywhere as in special instances, that in the experiment and in the natural process the point in question were merely quantitative differences, very frequently causes the overestimation of experimental proofs. This mistake affects experimental science as against that of observation, inasmuch as the latter utilizes experiments merely for conclusions which nature draws in long periods of time and in large—yes, enormous—numbers.

Cutting of the Gordian knot or the method of placing an egg upon its point by crushing the shell can impress only superficial minds; for to designate a forcible action—violence done to facts in order to bring about the final solution without laborious development—as the correct method and the result thus obtained as the solution of the problem testifies better than anything else how easily the human mind may be imposed upon by brutal facts, how great is the incapacity of the masses to differentiate between actual productions and mere assertions, how even indiscriminate striking which has nothing whatever in common with the solution of a problem, is nevertheless hailed as success and solution, whereas the attempt, or the advice, first to investigate thoroughly is never approved of, being considered an acknowledgment of momentary inability of mastering the problem. The impatient masses look for salvation in miracles and catastrophes; they expect of him who is to create an impression upon them that he directly interfere with the course of events, that he should disturb the quiet development of the latter, because

they wish to see results, respectively conclusions and points of rest, and wish to reap before the soil is prepared. The profound saying, "Nature does not advance by bounds and leaps," is foreign and incomprehensible to them.

Those investigators in the realm of medicine act in a similar manner who regard the complicated product of most heterogeneous reactive processes—*i.e.*, of such as merely indicate any form of change of the equilibrium, and that of the real regulating processes which influence the equilibrium only in the sense of preserving the normal condition, merely as a uniform action of defense, respectively as a process of regulation which should always be supported in this (presumed) direction. They endeavor, therefore, to influence—still in the stage of development (*i.e.*, of the struggle of the most various currents which create the equilibrium)—a series of extraordinary phenomena, the outer expression of which is the picture of disease, with one and the same remedy, at most with varying doses, and they even believe always to strike it correctly—*i.e.*, they demand almost the same miracle as a person who expects that against every attack of the opponent he is always protected by the identical parry corresponding to the supposed lunge. Does the only specific which we possess—*viz.*, quinine—cure the severe form of malaria, respectively all forms of malaria? Is even the most expert able to decide in the majority of the cases whether the symptoms presented by a patient suffering from diphtheria are signs of a reactive inhibition (*i.e.*, of the endeavors of the organism to restore the equilibrium), or whether they are abnormal irritations which are produced by the noxa, in which energy is wasted, therefore? Do we know whether the alarming symptom is an excess of regulation, the consequence of

most marked irritability to destruction and defense, or the yielding to the foreign irritations? Do we know whether the action of the organism is directed at the destruction or elimination of a toxin (irritation), or merely at the reduction of the irritability to the same? The stage of incubation—*i. e.*, the possibility of ushering in the manifold forms of reaction—is almost absent in the experiment, owing to the intensity of the effect, and we are here dealing with the relatively simple processes, created by enormous irritations (products of microbes), of an acute form of intoxication, since the microbes can not become transformed into histoparasites until after the lapse of some time; hence, the radically different results of investigators in the laboratory and of observers at the bedside.

Analogous fallacies—results, arisen in the laboratory, of the views regarding the simplicity of the solution of the most difficult biological problems—are offered to the experienced on every page of the history of medical science. The theory of the microbes represents one of the most conspicuous processes of this kind in the hands of hotspurs. If a micro-organism is merely a parasite which lives on waste, or, as a factor of symbiosis, is of at least equally as much advantage to the host as it harms him—most of the small living organisms vegetating upon the skin and upon the mucous membranes have this significance—it is purely accidental; it may be entirely insignificant to the economy of the host. If it multiplies only under certain conditions, perhaps like the benign *oidium albicans* in inefficient care of the mouth by patients suffering from acute diseases or by convalescents, like the pyococci in bedsores or the fungi which colonize in the pulmonary tissues in atelectasis of the

lungs, then it is a nosoparasite; for only a debilitated, diseased organism is capable of offering to it a suitable soil. If it exists in the blood, or if it has permanently lodged in the most important tissues, it is of itself a prominent sign because it demonstrates the weakness of the tissues. Yes, it may then even be the cause of the disease, in so far as certain injuries result only from its development; in these cases we may speak of histomycosis or hemomycosis (microbiohemia, mycohemia).

Types of these affections are: (*a*) Gonorrhoea, suppurations, tuberculosis; (*b*) anthrax, relapsing fever, and, possibly, malaria. But, naturally, the difference between histoparasites and nosoparasites (primarily and secondarily pathogenic microbes) is not as great as between mere surface parasites and parasites of tissues. Hemomycosis (mycohemia) constitutes a great danger, in so far as the enemy has penetrated, after overcoming all barriers, as it were, into the innermost recesses of the fort; however, according to the importance of the affected tissue and according to the greater or lesser resistibility, histomycosis also represents a great danger (endocarditis, multiple foci of micrococci in the kidneys, etc.). Especially dangerous is the transition from local to general mycosis (respectively toxemia), because it most strikingly demonstrates the increasing weakness of all possibilities of defense.

The danger, therefore, so long as the special activity of all parasites against the elements of the normal organism is not better shown than is the case at present, consists in the fact that—by any factor which diminishes the activity of the tissues or enhances that of the parasite—an ectosite becomes an endosite, respectively that an infection of the tissues is brought about by the prod-

ucts of microbes. That is the reason why all findings of this form of parasitism are of diagnostic and pathognomonic importance, altho it can not be denied that the local and general symptoms obtained by inspection, palpation, and by physical methods, as well as fever, etc., may also furnish quite as reliable, and sometimes even better, points. The demonstration of tubercle bacilli in the sputum is not as significant for the prognosis as the occurrence of hectic fever or the demonstration of many disseminated foci, of the continuous increase of a cavity, of traces of bright red blood which render an early hemoptysis probable, of disturbances of appetite, loss of strength, high-graded anemia, etc.

Therefore, the determination of the general condition—in which the finding of tubercle bacilli is to be valued simply as a mere symptom which only in connection with the others may tip the scales of prognosis one way or the other—is the aim and the basis of all endeavors at the bedside for a physician who does not consider his activity ended after he has established the name of the disease. The aim of a carefully examining physician, who does not intend to classify but means to prevent and to cure, is not the diagnosis as catchword, but the sum total (resulting from the examination) of information regarding the conduct of the energetic and the finding (resulting from this determination of the form of activity) of the means to remedy the disturbances. *Diagnosis is not a selfish end*, but a means; and only the endeavors made in diagnosis, which render it subservient to true medical purposes, are of value to the physician, however the scientific determination may be of interest to the investigator.

As previously emphasized, we can range the *comma bacillus* only in the first group; it is accidental, ecto(para)site, not even nosoparasite. The *tubercle bacillus* is the more unfavorable to prognosis and therapy, the more positively a histomycosis or of a symbiosis with pyococci (combined histomycosis, mixed infection) can be demonstrated from the sputum and from the other symptoms of the pulmonary or general affection.

The same significance is attached also to the *gonococcus*, which proves even by its presence in cells that we are dealing with a species of histoparasite. The question is only whether here a common pyococcus is enabled, by special weakness of the tissue (predisposition to urethritis, a particular irritability of the mucous membrane), to maintain the persistent form of urethritis, or whether we are dealing with an especially (primarily) active species which readily overcomes the resistance of the tissues. Clinical experiences and the difficulty of culture—as is well known, cultivation of the gonococcus requires special preparations—rendered the first assumption much more probable. The development of the microbe appears to presuppose a very particular facility of procuring nutritive material, so that only the most productive soil suffices; but it seems, on the other hand, that, after it has once become lodged, firmly established itself, as it were, it is unusually able to create for itself, by its products, so favorable conditions of further existence that it easily and for a considerable length of time places the affected tissues into an adequate form of irritation, a form of reaction which constitutes the tissue the purveyor of nutritive material for the endosite, without leading to exhaustion (death of the tissue), to adaptation, or to the early expulsion of the invader.

If under the influence of a noxa—which must not necessarily always be taken up directly by the digestive apparatus, but which may from the blood (absorption by the lymph channels or lungs) or by the route of the nerve tracts (nervous fever) cause an abnormal activity of the intestine—the lymph apparatus of the intestine are greatly irritated; if, we repeat, a considerable *change of the internal (tissue) activity of the intestine* (weakness of the tissue metabolism) exists,

which, as will be admitted even by bacteriologists, may also be due to other causes than merely to bacteria and their products, then benign microbes (for instance, bacterium coli or any species of cocci) may be very apt to become pathogenic (nosoparasites, endoparasites, respectively histoparasites), and add one or more new symptoms to the pathological picture. In this sense, therefore, intestinal ulcers in enteric fever would be only a secondary symptom, the expression, respectively the consequence, of a special condition of irritation of the intestinal follicles, and in this manner it would be easiest to explain why only a few ulcers of the intestine are present in a great many severe cases of enteric fever, whereas many ulcers exist in others and shape the picture more to that of an intestinal affection than one of a general disease (infectious disease). Here the original ectosite has become a histoparasite, respectively endoparasite, and may, by its products now circulating in the blood, also become a general noxa—*i.e.*, it may render the picture still more complicated, adding new features to the general disease. However, the histoparasite may also be only locally active, adding merely local characteristics to the picture.

It follows from the above discussion that we do not wish to look upon the so-called infection in enteric fever always as an intestinal infection (more correctly, an infection from the intestinal canal), altho intestinal manifestations constitute a frequent and distinct feature of the pathological picture, but naturally not the essence of the disease. In other words, in view of the still obscure etiology of enteric fever, we can only say that the disturbances are often most distinctly manifest in the intestine, or that the mucous membrane of the intestine participates greatly in the reaction to the noxa (excretion). However, there are numerous cases in which the disturbances of the intestine remain entirely in the background, whereas the nervous and pulmonary symptoms are remarkably conspicuous; a clinical fact which, with a certain justification, has been utilized in assuming an infection from the lungs; for the designation "typhoid pneumonia" may as well be the expression of localization as that of the etiological mechanism.

What, then, is gained with the demonstration of a so-called characteristic bacillus or coccus in excretions if the proof of its presence in the blood or in the tissues is not furnished? Nothing! What constitutes the proof that the microbium spunging outside of the organism is the cause or only a specific sign of the disease? Since disease or a pathological process can be assumed only after the essential part of the metabolism shows changes—mere alteration of the function of an organ, a deviation from the average type of the activity of an organ, does not in itself constitute a disease; since only that agent can be regarded as the active etiological factor, which changes the essential (internal) labor, and as pathological symptom only the functional change which depends upon an abnormality of the internal labor—the disturbance of the tonus of the tissue—the finding of microbes in the excretions does not suffice to demonstrate the pathogenic importance of these germs, but to accomplish this the proof is required that the parasite has become an irritant, an integral factor of the metabolism (a hemoparasite or a histoparasite). But this proof is usually lacking, and the micro-organism is stamped a generator of disease or an essential (pathognomonic) symptom solely by virtue of the following logic which, unfortunately, forms the basis of the majority of bacteriological deductions and of such significant interferences with individual and social life as are immediately based upon them with a great deal of boldness:

Major proposition: *I have not yet seen any case of cholera without comma bacillus* (diphtheria without diphtheria bacillus, gonorrhoea without gonococcus).

Minor proposition: *I call only those cases cholera in which the comma bacillus is found* (diphtheria, those with the

diphtheria bacillus; gonorrhoea, those with the gonococcus).¹

Deduction: *Cholera is caused by comma bacilli, diphtheria by diphtheria bacilli, gonorrhoea by gonococci.*

Many an adherent of bacteriological theories, when outside of the most intimate specialistic-scientific spheres, will perhaps understand this remarkably naïve form of bacteriological logic still better when he is reminded that, apart from micro-organisms colonized in the blood, the quantity of the microbes is almost never in a recognizable relation to the severity of the disease or its course; that the individual cases may present absolutely the same picture to the most experienced physician, whether they show microbes of a certain form or not, since the patients succumb or recover under exactly the same manifestations, are attacked isolatedly or simultaneously with many fellow sufferers in a certain time relation which, naturally, does not furnish a sufficient scientific proof for the assumption of an infection, altho it is always utilized for that purpose.

If we wish to employ a simple formula and designate the disease (form of reaction) as function, respectively as product of the irritation (irritamentum) and of the irritability, respectively disposition, (*P*); if, therefore, $IP = R$, then, if *P* is very slight, a maximum of *I* can, naturally, not be pathogenic, and, inversely, a minimum

¹ Hence, in the absence of the respective microbes, patients who die in a few hours under the classical picture of cholera, succumb to cholera nostras; patients presenting the typical clinical picture of severe diphtheria, die of some form of severe angina or of sepsis; individuals who for months show a marked purulent discharge from the urethra, with corresponding complications, suffer, in the absence of gonococci, from a benign form of urethritis; but persons with healthy lungs, whose oral cavities or sputa show tubercle bacilli, are tuberculous. It is well known that persons in whom no sign of physical disturbances can be found are counted as suffering from cholera if comma bacilli can be demonstrated in the stools, etc. The experienced physician, in all these cases, must make a different diagnosis and prognosis.

may call forth a great reaction if P is very great. Since generally two factors determine immunity, respectively predisposition—namely, the capacity of destroying irritations, hence to react to the irritation with increased internal labor, thus rendering it harmless, and the capacity of inhibition (*i. e.*, to prevent, by reduction of irritability, the irritant to become at all manifest), the equation naturally becomes more complicated; for the pathological manifestations then have two forms—one characteristic of destructive activity (on the irritant), the other of defense. Both may accomplish the end and are manifest in the different phases of the disease (crisis, recovery, convalescence), as non-irritability or intensity of the reaction, as symptoms of inhibition or irritation.

It is naturally very difficult here to come to a decision in a therapeutic respect, since an organism defending itself chiefly by reduction of irritability (inhibition) can not be identified with one that defends itself with increase of all activities, especially the thermic, and since we do not possess any reliable criteria to distinguish one form of reaction from the other.

Intensity and rapidity of onset of abnormal manifestations, therefore, are naturally not identical with severity of the disease (respectively with participation of the internal part of the metabolia); it can only be the expression of a particularly marked reaction, in a similar manner perhaps as powder and dynamite, upon the action of the same spark, will cause entirely different quantities of energy to become effective. In one word: *Not the intensity, but the form and importance of the reaction determine medical judgment (of the activity); the (visible) labor must in some sense be appropriate, respectively the ex-*

pression of endeavors appropriate to the preservation of the organism—*i.e.*, must contribute to the restoration of the disturbed equilibrium.

It is true, the intensity of the reaction may sometimes be only the expression of a particular intensity of the irritation; it may also indicate merely the promptitude and intensity of the measures of defense. The judgment of the physician is concerned only in the determination of these conditions—a decision which can not at once be rendered merely on the basis of the visible symptoms, of the external form of the reaction. As little, therefore, as a weak reaction is a sign of an insufficient defense, as little is a conspicuous one a sure sign of resistibility. To determine the value of the reaction for prognosis and therapy, we must know, above all, the direction of the reaction, whether it is caused by inhibition or by irritation, whether it is a sign of a particularly marked activity to destroy the irritation or a sign of defense (of the endeavors to reduce irritability). In the latter case usually the weakest (visible) reaction is the best; in the former, the most intense.

The *art of medical prognosis and therapy* hinges upon the discernment of this point. Unfortunately, we have lately again arrived at the point of seeing only defensive measures in all symptoms of disease, which is quite as false as if we would regard them as purely mechanical (quantitative, automatic) reactions—*i.e.*, processes which signify a wasting of energy, because the organism responds to extra-bodily irritations (processes of causation in the tissues that are useless to activity) as it does to the essential regulatory tissue and organ irritations indispensable to activity. (Compare the extreme fluctuations in the theory of fever, which are

merely due to the fact that no difference is made between *automatic* [*purely mechanical*, quantitative], and *appropriate* [qualitative] forms of reaction [functions]—*i.e.*, such as are advantageous to the continuance of the individual.)

Neither dare we at once look upon any and every abnormal constituent of the dejections (hence, foreign bodies—*e.g.*, bacilli, or any other unusual phenomenon, a so-called pathological symptom—*i.e.*, the abnormal expression of one of several organs) as specific of an affection, as pathognomic, or even as identical with it (as *ensis morbi*). We dare not at once construe an etiological connection between microbes and disease, even when a certain constancy of the manifestations particularly urges us to do so. Of course, a microbe may, as any other foreign and constant phenomenon, be in a logical and mechanical sense the cause of a complex of symptoms which we designate as disease in general or as a species of disease—characterized etiologically, or in some other manner specifically; it *may* be, we say, the cause or an essential factor, but it *must not necessarily be so*. At any rate, the proof of this connection must be furnished in a different manner than was done so far, since in the method employed until now the possibility is not excluded that what is a consequence or an accidental external expression of a process is regarded as the cause.

Not the presence of bacteria, but alone the abnormal forms of the reaction of the organism (of the tissues and organs) can create what we call *disease*. Not he is sick in whom bacteria can be demonstrated in the oral or in any other cavity (for their number is legion), but he who, in his tissues or in the blood, harbors smallest or-

ganisms which essentially change¹ the economy of the body and permanently diminish activity. Therefore, not he is affected with diphtheria from the organs of whose throat a certain bacillus can be cultivated, but he whose pharyngeal or nasal mucous membrane is in the well-known manner swollen, infiltrated, covered with membranes, and inflamed, whose general condition presents certain characteristic deviation from normal conditions.

If we were to look upon the presence of bacteria as identical with disease (or even as the first stage, as a prelude, as it were), then we should regard every plum as decayed upon the surface of which fungi thrive visibly in large numbers, or every healthy individual who harbors numerous pyo bacteria upon the skin or in the air passages (not in the tissues) as suffering from blood poisoning or as destined to become so. Then diagnosis, prognosis, and therapy—in short, the most difficult performance of medical acuteness and of medical art—would no longer depend upon inspection of the patient and upon the difficult judging of the condition of tissues, organs, and general strength, requiring the greatest care and experience, but merely upon the microscopical and bacteriological diagnosis of an investigator to whom the patient is of no significance—yes, who does not require

¹ Only he is ill whose internal labor is in a disproportion to the external one, in whom the equilibrium of tensions, the constant relations between the tonicity of the organs and tissues, which we designate as average tonus, have been displaced in favor, respectively at the expense, of one of the factors concerned, so that the visible labor of the organs for displacement or tension of the masses, the extra-bodily (endosomatic or exosomatic) labor, is diminished, whereas the labor of the tissues is increased, or *vice versa*; a condition which must lead to a stagnation of activity, since the absorption of material depends upon the labor of the organs, the development (transformation) of energy upon the labor of the tissues.

any medical knowledge, or no more than a weather prophet who merely consults thermometer and barometer wants meteorological acquirements.

This modern form of diagnosis, prognosis, and therapy *in absentia* or *in partibus* is an unsuspected completion of the old saying that the half is more than the whole, since here not even an inspection of a large part of the body is required, but a particle of an excretion, which is not even a part of the body, suffices for a positive opinion as to the condition of the whole body, the condition of the forces of which, after all, should form the basis for diagnosis, prognosis, and therapy.

In connection with these discussions, it may not be out of place to say a few words regarding the *theory of infection*; for, in our opinion, here also the situation has not become any clearer now, altho it appears to be so, because the observers, from the very beginning, gaze at the processes through the spectacles of a theory, or they draw conclusions of analogy that are too far-reaching. Thus many a fallacious theory has for long periods attained the reputation of a well-founded truth.

It is often thought possible to conclude with certainty from the successive affection of a number of members of one family upon an infection from case to case. But there is much to say in favor of the fact that here, too, we are often dealing merely with the expression of a reaction which varies, and hence does not manifest itself at the same moment to one and the same noxiousness (possibly continuing to act in diminishing intensity, or, upon the occurrence of a distinct affection of the last members, already extinct—early and retarded reaction). In those persons who are possessed of the greatest

predisposition (especially capable of reaction) probably only the external disturbances which we erroneously designate as the onset of the disease occur first, whereas the others show these phenomena—*i.e.*, fall manifestly sick—only successively. As these phenomena must naturally have a previous history, as, therefore, the absence of visible manifestations (of the symptoms produced only by changes of the extra-bodily labor) does not constitute a proof that the tissue energetic (the essential, internal, labor) might not have been considerably affected for quite a time, we can not, from the moment of manifest affection of adults, at once deduce the length of the period of incubation, or, more correctly, determine solely from these data the moment of the first disturbance of the system (which may, but must not, lead to the specific disease), all the less since very often it is not a question of an acute effect, but of an accumulation of the injurious influences or of a gradual disturbance of the organism, which in particular is fraught with danger (asthenic reaction).

We can probably speak of an unquestioned infection only when, for instance, with the positively determined absence of endogenous typhoid-fever cases in a certain locality, the arrival from abroad of an individual who is already affected with manifest symptoms, or in whom the incubation stage of the disease has already developed (within the regular incubation period), is followed by affections of his immediate environments (of the nurses, but by no others). Even then the possibility of an accidental occurrence can not be excluded, but this is so very improbable, according to human conceptions, that such well-determined cases may be looked upon as positive proof of the possibility of infection from case to case.

However, if even a few cases only of an identical affection (typhoid fever, or other so-called infectious diseases) have been observed in the same locality at the time of the arrival of the manifestly affected person, respectively of the person in the preliminary stages of the disease, or a short time previously, or if, simultaneously with the affection of the nurses, identical cases are determined in other localities, even then the apparently striking fact of the nurses or relatives being taken sick can no longer, in a scientific sense, be utilized in demonstrating the infection, respectively introduction; for in localities in which only *one* autochthonous affection of the same character occurs, there exists also a possibility for every inhabitant to become affected. As probable as is the assumption that the patient's nurses who became afflicted in the same manner were infected by him, still this condition can not be utilized with scientific certainty until all other possibilities have been excluded, and this is frequently not as easy as it appears, as, indeed, the theory of infection is almost as difficult as the explanation of the fact that relatively only few of the combatants are struck down in a hail of bullets.

Since we assume, only in consequence of many years of experience, regarding the influence of *predisposition*, that diseases are brought about much more rarely by direct transmission of toxins—respectively, microbes—than by gradual or sudden effects upon the activity of the body in consequence of changes of the external factors, of the vital conditions in the widest sense—especially of the finest currents propelling the smallest machines of the organism (the energetes), which, however, must not at all be identified with electric ones—since, therefore, we consider transmission from case to case comparatively

rare, it seems to us that *strict isolation* of the patients in so-called infectious diseases is far less important than *hygienic* measures, eventually the removal of those not as yet affected. But even this step promises success only when the injurious influences have not acted yet or only for a short time (see above), and when the disease is not endemic—*i. e.*, if the factors are active only locally, perhaps in one house (or a limited district), as is frequently seen in diphtheria, typhoid fever, cholera, etc. In the opposite case, naturally, danger can be avoided only by removing to a great distance from the infected locality, not by simple migration from one room or house to the other, in the same manner as we are safe from lightning only after we have left the zone of the storm. In other words, not the intercourse with the patient is dangerous in many cases, but the sojourn at a certain place, in which case it is not impossible that disease of many occurring in the same rooms may enhance also the injurious influence of the place, either by exertions during the nursing of the sick, or by emotions, or as a result of an influence upon the atmosphere by exhalations.

Even admitting the special pathogenesis of the microbes in many cases—in part, it is true, solely with the supposition (see above) that the body had been previously weakened by some form of influence or is kept in a condition of irritation (in short, becomes predisposed, induced, to react to microbes differently than was previously the case)—it does not follow that we must admit *disinfection* to be appropriate or efficacious. If we assume, for instance, that a certain moisture of the walls, or exhalations of the soil, cause a disposition, maintain a certain condition of weakness, and that for this very reason a frequent development of angina or diphtheria

takes place—*i.e.*, according to the bacteriological conception that pyococci or specific bacilli—introduced from somewhere or ubiquitous—now more readily multiply, respectively colonize in the tissues, then, naturally, the removal of the inhabitants would be the radical prophylactic measure, but with a prospect of permanent success only provided that, upon their return, they will find different¹ external conditions. Probably nobody will believe that pyococci or bacilli can be destroyed, since the hosts themselves are their carriers, and since the radical extermination of the parasites of the cavity of the mouth would be identical with the destruction of the mucous membrane of the oral cavity.

Even clinical investigation up to the present has furnished enough points that the rôle of the microbes as primary generators of disease, and thus as a pathognomonic sign in the true sense of the word, is of by far less importance than was assumed even by skeptical minds; also that microbes can not play a very prominent part just in the most important infectious, or, more correctly, epidemic diseases (measles, smallpox, scarlatina, syphilis, etc.), since their presence can not be demonstrated, notwithstanding all the aids at our command. Hence, unless we wish to assume that these microbes are not accessible to any of our present culture methods, and that new ones must be found for them, then this fact must be considered proof that microbes are not always the sole generators of disease, and that infection may be brought about in some other manner—*e.g.*, by *exhalation of an active volatile albuminous body*, or—in syphilis and gonor-

¹ It happens frequently that children that are taken to another place to avoid infection, become affected immediately after return into the disinfected residence.

rhea—by some form of serum, the preparation of which requires only a living body, but no longer a microbe. Infection is possible as soon as a serum product is capable of entering into another organism and of producing abnormal reactions in the latter (inoculation). The existence or continuance of diseases of this nature is no more wonderful than the fact that no more equivocal generation occurs under the present conditions.

The questions, therefore, which are considered solved according to the opinion of bacteriologists, remain unanswered in their fullest sense. Scarcely one of the many problems of etiology, predisposition, and prognosis is solved, and yet it is a most amazing condition of affairs that, overrating the certainty of the new standpoint, confirmations of the correctness of the new views are no longer looked for, but endeavors are made even to utilize the theories of the causal importance of microbes which are not at all proved yet, or only in a very insufficient manner, as a touchstone for the correctness of the experience of a thousand years.

XXI

OROTHERAPY

I

NO EXPERIENCED physician who is familiar with the changes of medical fashions and with the customary misleading, but still effective, demonstrations in the realm of therapeutics will for a moment doubt that orotherapy will have an all the shorter lease of life the greater are the hopes engendered by it in the minds of the contemporaries. Altho, therefore, the verdict regarding the value of this method may calmly be left to time, still this does not relieve us of the obligation of briefly formulating even now the objective scruples, arising from scientific and practical experience, against the method itself, and, above all, to protest against the manner of its introduction into practise. What is still to be proved is already accepted as demonstrated, and a remedy which is yet to stand its fire ordeal in practise, and can have stood it only after years of trials, is lauded as a panacea because it is claimed to have acted successfully under entirely insufficient conditions of test. . . . The point is already reached that the adherents of calm deliberation are accused of inhumanity because they do not consider *therapeutic interference at any price* justified, but only interference that is *necessary*, and because they

demand scientific guaranties for the efficacy of the remedy, which, naturally, can not be obtained, owing to the tests made at an accelerated pace and in the bustle of the market.

Because some investigators believe, after many experiments on animals and some trials in human beings, that they have found a safe remedy against diphtheria, now healthy children are also to be submitted to this method by compulsion, as if *every* child of necessity would fall a prey to diphtheria, as *if the affection of several children of the same family by this disease constituted the rule and the cure of the malady by the methods so far prevailing the exception*, or even an impossible event.

Have we quite forgotten that the average mortality of diphtheria in private practise is scarcely 20 per cent. when we consider long periods and the fluctuations of the different epidemics and endemics, and that, if the doubtful cases of simple throat inflammation are counted in—which are permitted to figure as diphtheria only in therapeutic statistics or for other opportunistic reasons—it is still considerably less? Even the statistics of hospitals, which under ordinary conditions receive only the so-called severe cases, will probably show not more than from 40 to 50 per cent. of deaths. The percentage of mortality must naturally be considerably less if, as is customary to-day, not the characteristic membranes in the throat and other organic disturbances, but the *diphtheria bacillus* is looked upon as the basis for decision, leaving scarlatinal diphtheria, which is caused by other microbes, and which otherwise furnishes an essential part of the severe cases, completely out of consideration, because here the serum is not effective.

Gratifying as it is to the philanthropist to observe

that an appeal to humanity opens not only the hearts but also the purses, it should be borne in mind that the introduction of this heterogeneous view-point for scientific examination creates a forced condition for the patient, for his relatives, and for the physician, than worse nothing can be imagined. Such a forced measure to treat all cases alike after a certain method, without distinction of the individual case, we might possibly consider justifiable from our standpoint if the method had stood the test of time, if, above all, its *harmlessness* had been demonstrated, and if the catchword "diagnosis" were identical with the actual recognition of the processes in the organism.

However, these requirements have not at all been complied with in the case in question, and for this reason let us attempt to put ourselves into the position of the relatives of a child affected with an inflammation of the throat, and into the position of the physician who, even with the greatest experience and upon the most careful examination, can not for the time being decide whether diphtheria or a benign inflammation of the throat be present. As a conscientious man, he confronts an unsolvable enigma, since consideration for the anxious parents who look upon the serum as the only and allegedly certain remedy to save their threatened children, urges him to accede, or to agree to an opportunistic diagnosis and therapy which burdens his conscience with a grave responsibility.

If he does not inject, because he is convinced that the case is a simple inflammation of the throat, he will undoubtedly be always accused—in case diphtheria should develop, as happens so often in doubtful cases, and take a fatal course—of having recognized the danger too late.

But if he does inject, to escape this reproach or being misled by his own anxiety, even in doubtful and simple cases, then he renders himself guilty of a deception in that he aids in establishing and furthering the efficacy of a remedy in cases in which no proof whatever of this efficacy is furnished.

Objection will now at once be raised that this falsifying of statistics does not signify anything in comparison to the advantage accruing from the saving of a few patients injected in proper time and possibly saved by this injection; but we must, on the basis of our conviction, contradict this very objection, above all. If the adherents of orotherapy, who among themselves even are not quite in accord as yet regarding the value of their own preparations, maintain that the injection is absolutely harmless, they show with this contention merely a peculiar misjudging of the situation, and again prove how wrong it is to apply the conditions of the experiment to the state of affairs at the bedside.

Bacteriology is bound to arrive at wrong conclusions by the very fact that it places man upon the same footing with experimental animals and dead nutritive soil (of the cultivation apparatus)—*i. e.*, in that it almost entirely eliminates the individual peculiarities of the organism by application of most intense irritations and setting aside of all protective arrangements (injection of large quantities of pure cultures into the blood). Bacteriology can not, like the physician at the bedside, reckon with the changes in the course and the continually new combinations of the infectious disease, but it is able to utilize as the object of its studies and as a basis of its deductions only the uniform picture of the injection disease (the flooding of the organism with microbes and their products).

Therefore, the result of experimental investigations is the perplexing fact that animals poisoned by injection not only become affected in an equal manner throughout, and, without treatment, die, but without exception they are cured with one dose of a (or, more correctly, *the*) remedy which is measured merely according to the body weight. Observation at the bedside, on the other hand, continually surprises even experienced physicians by the diversity of the manifestations of the pathological process and by remarkable facts which explain in particular the extraordinary significance of individual conditions in reference to the therapy to be adopted. In situations, therefore, in which even the fundamentals of observation are so very different, particular care should be taken regarding conclusions, and we should endeavor to refrain from the utilization of unfounded, because exaggerated, conclusions from analogy as the basis of our medical actions.

We know of no efficacious remedy which, analogous to the substances employed in the animal experiment as curative potencies, could be used in the same manner in all human beings without deleterious by-effects. Possibly fifty persons of one hundred possess the same susceptibility, whereas, unquestionably, the most varying degrees of susceptibility prevail among the remaining fifty, and if among these fifty are even five only who react to a remedy in an unexpected form (*i.e.*, with disagreeable or dangerous symptoms), a physician assumes not a small responsibility who incorporates such a remedy into the organism without urgent cause—especially into the infantile organism, for which it does not constitute a remedy, but a severe danger.

All these considerations apply in a special measure to

orotherapy, because here a foreign, energetically acting, albuminous body reaches the interior of the body in the most direct manner, taking it unawares, as it were, with evasion of all protective apparatus. The danger of an injurious effect, therefore, is especially imminent, and it is not excluded if the injurious consequences do not occur immediately. The harmful effect need, for the moment, not be conspicuous at all; it may take weeks, months—yes, even years—until the first manifestations of an injury of the body become plainly noticeable. It is well known that in a number of particularly severe infectious diseases the disturbances do not take place for weeks—yes, months; after the introduction of the infective substance they may recur for several years, and finally lead to a rapid decline.

Many of the remedies in use to-day, in their permissible maximal doses, are harmless for the majority of adults; nevertheless, a physician will observe great care before administering to every adult, let alone to the delicate organism of a child, the permitted maximal dose at the first time, before having satisfied himself of the individual (average) susceptibility to the remedy. How many persons have been greatly injured by antipyrin and salicylate preparations—under some circumstances most beneficent remedies—because the individual susceptibility had not been considered! Should healing serum alone establish an exception to these experiences, and be harmless in all individuals and in all degrees of sickness in the same first dose? At any rate, the fundamentals of orotherapy betray the same misjudging of all previous experience at the bedside, and the under-rating of individuality, as the original Koch method, the treatment of tuberculosis with tuberculin, the failure of

which for the same reason could not be doubtful to the experienced physician from the very beginning.

It appears, above all, therefore, that the dose of the serum hitherto recommended is very large, and, even altho up to now no immediate harmful effect of these large doses has been noted, it should at least be considered that the serum is derived from horses which probably do not represent the most costly and most valuable examples of their tribe. But even if only healthy animals are selected, it is probably safe to assume that, in the carrying out of their occupation as preparers of the lymph, their health will not be permanently preserved, since *before they are thoroughly immunized* they must pass *through repeated attacks of a severe infection or injection disease*, and, besides, are in a *stage of convalescence, or, after their full recovery*—if immunization and recovery may be placed upon an equal footing—*are weakened by persistent bloodletting*. What would be thought of a vaccinating physician who takes lymph of a child just recovered from a most severe attack of diphtheria and under the influence of repeated venesections?

Hence, it would be important, above all, to know how the nutritive condition, the strength, and the length of life of the purveyors of serum will be in the future. This statistical report would be vastly more important than the daily bulletins from hospitals or from private practise, furnishing the astonishing statement that once again a patient suffering from severe diphtheria had recovered under the application of the serum, just as if the cure of most severe cases had not been observed before. It should be considered, further, that the protective agency of the remedy, as may be gathered from

theoretical reasons and as is admitted also by its adherents, can, in the most favorable case, extend only over a few weeks. Would it be possible that a child who, in the course of a year, has half a dozen attacks of inflammation of the throat, should be inoculated as many times? Is it believed that this repeated inoculation would proceed without harm? Furthermore, is diphtheria the only disease by which children are endangered, and how are we to act if remedies obtained in the same manner are recommended with the same enthusiasm against the other diseases? Will it then be necessary, in a family the children of which have simultaneously scarlatina, measles, and diphtheria, that all three remedies be employed at once? We shall not dwell upon these questions any longer, but we believe that it would probably be better in doubtful cases to let nature help itself, and, by hardening and strengthening of the organism, to create a natural protection, not against the disease, but against the lasting influence of the noxa once taken up.

It is not any more possible to prevent the affection of single individuals as it is possible to avoid wounds by shots in war. This can not often enough be emphasized, since we are, after all, dependent upon the outer world, and can not—probably to our own benefit—hermetically seclude ourselves. But it is not doubtful that an otherwise strong and healthy body not injured by treatment is better able to overcome even dangerous wounds than one that has been weakened. From this it follows that the doctrine preached by the true hygienists of all times that not the fear of infection and external influences, bacteriophobia and effemination, is the goal to be aimed at, but strengthening of the organism and

adaptation to the most various conditions of life, which also include pathogenic influences.

Therefore, we arrive at the conclusion reached by us in several previous articles that a prophylactic treatment by inoculation is *possible*, it is true, but *uncertain* and of *short duration*, and that it must carry more harm than good in its train, since we are not familiar with the correct time nor the proper object for its employment, nor yet the injurious effects that it carries with it in other directions. But since, fortunately, only a fraction of the children succumb to infection by diphtheria—and in by far the majority of families only one child becomes affected¹—and since of this fraction again only a small portion falls a prey to the epidemic—for, as is well-known, extent and intensity of the various epidemics are very different—we must not, in order to protect a few individuals with a degree of possibility, expose all humanity to the influence of a remedy the curative action of which is not less subject to doubt than its harmlessness.

If it is further considered that a severe general disease is often the consequence of common (smallpox) inoculation, in which only a *minimum* of lymph of healthy calves is introduced, may we then be certain that *two hundred or three hundred times the quantity of the serum of anemic horses, which have repeatedly passed through severe attacks of*

¹ William H. Welch, the well-known Professor of Pathology in Johns Hopkins University, states in a very remarkable article ("Bacteriological Investigations of Diphtheria in the United States," *The American Journal of the Medical Sciences*, October, 1894) that, in a series of 113 connected cases of pseudo-diphtheria observed in 100 families, *only in nine cases more than one case occurred in one family*, whereas a group of 70 cases of true diphtheria affecting 50 families *showed more than one case only in thirteen instances*. (Pseudo-diphtheria is distinguished from true diphtheria with which it has the clinical symptoms in common, only in that the Löffler bacillus is absent.)

poisoning by injection of the diphtheria bacillus and its products, exerts only a favorable effect?

We have here mentioned only some of the objections which should be qualified to dampen the enthusiasm regarding the new method; a second group is evolved from the criticism of the proofs concerning the efficacy of the new method.

II

How is it with the healing action of the inoculation in cases of the disease already being developed—*i. e.*, demonstrable to our observation? It is probably plain even to every layman that a disease which is already distinctly characterized by a number of symptoms, by distinct general manifestations and tissue changes, must possess a previous history. It is safe to assume that a great chain of processes had developed in the organism a shorter or longer time before the outbreak of the disease, or, more correctly, before the symptoms that we are capable of observing become manifest (hence, even before the stage of so-called incubation).

However, if a whole series of processes has already been called forth which, even independent of the first process of liberation, continue to exist and to act, the conditions for the possibility of an influencing and restoration of the former state, hence for real treatment, naturally show a phase that is different from the previously mentioned method, the protection by inoculation, the nature of which consists, after all, only in the prevention of infection. It is intended, by the introduction of minimal quantities of the inoculation virus—a substance related to the generator of the disease, which is

modified in a certain manner but is foreign to the body—to frustrate the subsequent influencing of the body by stronger irritations of the same kind, perhaps similarly to a body gradually habituated to the effects of cold (hardened) after a certain period of adaptation becoming insusceptible to very considerable changes of the temperature.

As a protective remedy (before the affection) a minimal dose of the lymph may be efficacious, whereas in a diseased body—hence, already under the influence of maximal irritations of the same origin—antidotes must naturally be administered in much larger doses, quite apart from the fact that, as previously stated, entirely different conditions have been created, and points of attack for therapeutic measures, after the affection has once taken place. But how, the question arises, shall the relatively small quantity of horse serum—*i.e.*, small only in proportion to the quantity of its own serum—act curatively, since the infected body, which has passed through a similar process—only under much more favorable conditions—as the animal furnishing the serum, is not capable of forming from its own serum, under the influence of the same carrier of infection, the healing potency in sufficient quantity?

Accordingly, the trend of thought of the orotherapist with reference to this point is as follows: Whereas a great portion of those that are affected finally develop their own serum and become saved thereby, another portion is able to accomplish this only with difficulty or not at all, and, therefore, unquestionably requires the support rendered by the inoculation remedy, either in that this in itself represents the antidote or in that it qualifies the diseased body to produce the same.

But since upon the amount of susceptibility of the patient and upon the severity of the changes in the economy of the body manifested by the affection depend the possibility, certainty, and form of our interferences, and since we are unable to know the category of cases to which a person belongs who is already affected, it is safer to make the injection in every instance with the same large dose as early as possible.

This theoretically correct deduction resulted, therefore, in the apparently justified demand to inject the serum as early as possible—if practicable, on the first day of the disease. However, this demand withdraws from the examining physician, in the present state of our knowledge, *the safe footing for judging the case*; a method that is efficacious only under such conditions loses all characteristics of a remedy and is from the very beginning stamped a (prophylactic) inoculation protective, and, in the hands of enthusiastic therapeutists, a miraculous remedy (cure-all).

A rapid and convincing determination of the value of an inoculation protective is absolutely impossible; it is feasible only after years of testing over very much extended territory and under all conditions, to exclude every accident and to deduce the efficacy of the remedy from the distinct, constant decrease of the mortality and morbidity of diphtheria during a long period. The favorable results of the moment are entirely without significance for this purpose, as here success must be weighed, not counted. Ten favorable results are not equivalent to one unfavorable one. For the former have probably been accidental, since the severity of the case can not be estimated at the onset, and because untreated cases were in the majority; but an unfavorable

termination shows the limits of the efficacy of the method with certainty, whether it is a question of insufficient protection by inoculation or of deficient curative action. There is no foundation for the contention that one case of diphtheria is bound to be followed by further cases in the same family or in the neighborhood; who, then, will be bold enough to maintain that nothing but inoculation under these circumstances had protected the relatives from the affection?

But the difficulty of demonstrating therapeutic determinations, on the other hand, can not be estimated too highly, either; for the intensity of the phenomena is neither proportional to the severity of the disease itself, since a great many of the internal disturbances remain hidden from us, nor do the visible and apparently threatening manifestations always continue to develop in a corresponding manner. Besides, a certain form and intensity of the clinical symptoms may be produced by quite heterogeneous causes—the condition in true diphtheria, allegedly alone curable by serum, is, in our experience, in many cases exactly the same as in scarlatinal diphtheria, which is caused by entirely different microbes; and apparently equal, even mild, phenomena at one time carry with them the conditions for the continuance of the process, at others even the conditions for retrogression (cure).

Any one who employs a certain method in every case of fever, without considering the fact that many febrile conditions last but one day—yes, even only a few hours—will be able, in the eyes of the believing, to record great therapeutic results, it is true, but scientifically he has not proven anything regarding the efficacy of his method. At any rate, he blunders against the first principle of

medical activity not to interfere *without urgency*, since unnecessary interference is often harmful, or may sometimes counteract the natural efforts at cure in the organism.

To inaugurate treatment on the first or second day of the affection means, therefore, to take a leap into darkness, and to treat indistinct and often insignificant, rapidly passing disturbances with the same energetic remedies as well-developed, lasting, pathological symptoms. But under no considerations must a remedy be regarded as indifferent, to which such great efficacy in marked disturbances in the body is attributed, and which undoubtedly possesses the quality of a great irritant. It is probably quite safe to assume that the superfluous employment—*i. e.*, undertaken in an organism that is not infected—of larger quantities of the inoculation virus—a substance, therefore, which is claimed to be capable of neutralizing the action of large amounts of generators of infection and of their products—will be capable of exerting similar disturbance equivalent to that of the infection itself, altho, as it were, in an opposite direction.

The difference between the elements causing the protection by inoculation and those which are regarded as remedies against diseases, as well as the conditions to be fulfilled by an inoculation or a therapeutic means, may be illustrated by an example simple enough to be appreciated even by laymen. As is well known, fire and water have opposite effects; hence, water may be looked upon as a protective means against conflagration, and also as a curative means in cases of inflammation. We all know that it is easy to guard a combustible article—such as paper, for instance—against igniting; but it is difficult—yes, impossible—to subdue, with the

same, and even with a larger, quantity of water, an inflammation once started or raging in the deeper layers. Altho, after the lapse of some time and by the employment of relatively large amount of water, the fire may be smothered, the inflammation subdued, this is not sufficient to preserve the inflamed substance, since a great deal of the material is already destroyed or greatly changed.

Here we have a far-reaching analogy to the three possible forms of therapy: protection from disease, abortive treatment, treatment of the well-developed disease— analogies which would be complete were it not for the processes constituted somewhat differently by the peculiar form of combustion in the organism (slow combustion, according to M. Traube), and by the regenerative power of the body. The organism, namely, is capable of equalizing even considerable visible changes; of retransforming, as it were, into normal material the parts only singed; it is true, those that are charred entirely even the organism can not restore, but it can partly replace them by new formations.

We are capable, therefore, of conferring upon the body some form of undoubtedly brief protection by inoculation, in the same manner as combustible material may, for a brief period of time, be rendered fireproof by sprinkling with water. However, not every substance will bear sprinkling, or even frequent moistening, with water without being severely injured, and in the same manner will inoculation not protect all persons who are vaccinated, or even permanently guard them against disease; in fact, it will be fraught with more or less danger to many. (Water, under certain conditions, may even serve to intensify the firebrand, as will be readily seen when a certain amount of it is thrown on burning coal.)

We are further capable, also, of readily subduing a conflagration so long as it is localized to the surface; we are generally in a position of controlling an affection so long as no change in the tissues has taken place, so long as the irritation has not taken a firm hold. Water is not capable, after the fire has been subdued, of restoring the former (normal) condition—*i.e.*, of rendering the original state to the material; hence, it is not a remedy in the proper sense, but only a means to prevent the liberation of certain changes and to restrict the intensity of the influence. But healing means not only to subdue the fire, but to restore the former condition to the substratum, which in a certain manner had been changed by the process of inflammation.

The best example of such a disease in which the real tissues of the body, the less accessible parts, are not yet affected is offered by the milder forms of malaria, and hence this instance is always quoted when an era of specific and prophylactic (inoculation) therapy looms into view.

The conclusion that, as we possess in our pharmacopeia an efficacious remedy against malaria (*viz.*, quinine), also a specific—*i.e.*, operative in every instance—inoculation remedy might be found can be met by the following objections:

(1) The generator of malaria is distinguished from all known pathogenic agents, in that it causes changes of the tissues to occur conspicuously late, owing to its localization in the blood or in the spleen. This is the reason why malaria is readily curable, or accessible to therapeutic measures, even after having existed for many months.

(2) Quinine is effective only in the milder forms of

malaria, in which changes of tissue in the true sense of the word have not occurred yet.

(3) The dose of the drug varies according to the individual.

(4) Quinine, looked upon as an irritant of the body, is disproportionally weaker than an albuminous substance originating in a foreign body.

(5) The deleterious effect, or the eventual idiosyncrasy to quinine, is essentially lessened by its absorption from the stomach; hence, is able to exert a much more inferior irritation than if it were incorporated through the blood.

The above comparison evinces the differences between remedies in form of inoculation and other remedies, and also that the points of attack and the aims of both are different. It is further evident that protection by inoculation is possible upon application of most minute quantities of a certain remedy, but that every protection by inoculation is fraught with danger which is the greater the less the inoculated person is predisposed to a certain form of infection, and the more susceptible, therefore, he will probably be to an irritation acting in the opposite direction. It will also be conceivable that the cure of fully developed disease can not be accomplished even with much larger quantities of the substance acting as protective agency, because it is no longer a question simply of destruction of the causes. The infection, even before the pathological picture is well developed, has called forth a chain of processes which, once present, can not be removed by agencies acting in a direction opposite to the first cause, but only by qualitatively different influences to be determined in every individual instance; hence, a substance can act as a true antidote only so long as the pathogenic element

has not yet liberated that form of changed reaction which, under all influences, is peculiar to the individual. Magnetized iron can not be demagnetized by magnetism of the same or of the opposite form; and even if the action of the acid may be neutralized in that an alkaline substance is speedily brought in contact with the affected point, this holds good only for that brief period of time during which the acid has not as yet called forth an essential change of substance by transposition of the parts and by other combinations.

This is not the place to enlarge further upon these comparisons and to show how the insecurity of the *theory of the toxins or antitoxins*¹—the latter barbarously designated “antibodies”—which forms the basis of modern inoculation therapy. The doctrine of poisons and antidotes has always played a prominent part in medicine without ever leading to the discovery of the nature of an antidote and when a substance may be active as such. Neutralization in a chemical sense can be spoken of only with reference to the test-tube, but not in connection with the human body (or only under certain conditions—*i. e.*, upon a superficial and temporary action). It is true, so soon as chemically acting substances (such as acids) have formed combinations with the components of the body, they may be separated by equally powerful

¹ If the modern theory of the formation of curative antitoxins (antidotes) through the action of the toxins really possesses the significance attributed to it, it follows that the serum of the alcoholic or of the morphinist must be one of the best remedies against alcoholism or morphinism. Possibly we may live to see such a method of treatment call a halt to the ravages created by these two aberrations. The point in question would then only be which animal species would be the best purveyors of serum, or whether it would become necessary to rear a few specimens of alcoholics or morphinists, to be on the safe side, in order to cultivate and obtain the serum. This sarcastic prophecy has come true (to our sorrow) in that, according to the reports in the daily press, a serum against drunkenness has actually been recommended.

substances (alkalis) possessed of the opposite qualities, but the peculiar susceptible (most labile) equilibrium of the parts characterizing the machine of the organism will in every instance be permanently disturbed under so marked influences, so that neutralization can not by any means be considered equivalent to a restoration of the normal condition or even to a diminution of the disturbances.

But if in infection and also in protection by inoculation we are dealing besides with chemical effects, with agencies also which we designate as mechanical ones (hence, with stimulation of special forms of motion and vibration in the most minute parts of organic tissue), then we can no longer speak of a successful action of chemical neutralization, because the more marked movements of the parts, once ushered in in one direction, at once calls forth further changes, the extent and direction of which are unknown to us; conditions, therefore, the influencing of which in the direction known to us—hence, the one which we are alone intent upon attaining—is, to say the least, doubtful.

III

We must forego the further elucidation of the fact that protection by inoculation and recovery (artificial or naturally acquired immunity) can not—at least, not primarily—depend upon the formation of certain chemical bodies influencing the organism in an opposite direction or even neutralizing one another, but that immunization is based upon the same physico-physiological process as are the numerous other phenomena pertaining to the domain of adaptation or practise. The capacity of an

organ to adapt itself—*i. e.*, to accomplish, according to circumstances, the minimum or maximum of external or internal labor under the influence of certain effects represented by the outer world—constitutes the main condition of persistence in the struggle for existence. Daily experience demonstrates the full significance of this factor in the methods of hardening against external influences, and in the rational training of sport-loving humanity. The farmer and the mountaineer with impunity expose themselves to harmful influences which would unfailingly cause severe catarrhs to the dwellers in cities and to the stay-at-homes. The practised gymnast is able to master tasks, the solution of which would expose the tyro to the greatest dangers. Every one knows that the muscles of a weakling who attempts to lift a heavy load may be seriously injured without the formation of a pernicious substance (toxin). It is also well known that gradual, rationally increased demands may enable even weak muscles to perform a considerable task, without the formation of a substance that acts in an opposite direction (antitoxin) coming into play.

All these considerations are meant to evolve the theory that adaptation to certain irritations must be promoted, above all, by an increase of the physiological capacities, and that a remedy or an agent of inoculation may occasionally, it is true, afford protection from the pernicious influences of powers acting suddenly and in abnormal quantities (in whatever form they may be manifest), but that this protection is uncertain, whereas the frequent repetition of such aggressions is bound to result at last in the destruction even of a well-organized body.

Let it not be quoted that an exhausted and weak individual is capacitated to renewed activity by the admin-

istration of more intense irritations (also aimed at by inoculation)—for instance, by a large dose of alcohol—and that he is enabled to attain the result he is striving for, the aim of his exertions, and, with it, his preservation; for the conditions here are entirely different, since it is merely a question of only one performance. But the dangers from which inoculation protects must be overcome more than once, the body being constantly surrounded by them. Even he who knows the advantage of a large dose of alcohol will not advise the frequent repetition of this remedy which, besides, answers its purpose only when the aim is nearly reached, or, to carry the comparison still further, when cure is not difficult.

Modern orotherapy which, after the conspicuous failures of anti-bacterial (microbicide) therapy and of the Koch method, again begins a new triumphal procession through the realm of statistics, is therefore built only upon the neglect of the significance of individuality and upon the misjudging of the essence of disease and cure; for it identifies the conditions of animal experiments with those of disease and confuses the possible—but not always efficacious or even beneficial—preventive therapy (inoculation) with the possibility of influencing pathological conditions, the changed forms of reaction of the tissue occurring only after continued action of the irritant.

According to our opinion, the various forms of inflammation of the throat are differentiated regarding the danger of the condition less by the nature of the irritant, the species of the so-called pathogenic agent, than by the extent and form of the reaction of the affected tissue. Only streptococci or pyococci are present, for instance,

in scarlatinal diphtheria, but the cause of the affection is not any more favorable than that of specific diphtheria. But as the same microbes are found also in simple, benign, inflammation of the throat, the benign or malign character of the disease can mostly be due only to the capacity of resistance of the tissues, to the so-called predisposition of the affected individuals.

The new treatment of diphtheria, in reality sister to much-slandered homeopathy, supposed to be especially effective in cases which are treated on the first day—*i.e.*, at a time when the clinical symptoms do not yet permit of a positive diagnosis between benign inflammation of the throat (amygdalitis) and diphtheria, when, therefore, the diagnosis can be based solely upon the presence of the specific bacillus. However, such a conclusion can be declared justifiable only if the mere presence of diphtheric bacilli were identical with the condition of being affected by diphtheria, or if the finding of the bacilli would furnish even the slightest criteria for the severity of the process. But, as a matter of fact, only the well-developed tissue changes, or general manifestations are the sure signs of a disturbance—*i.e.*, of the action of an irritant having taken place upon the tissues, and, therefore, they are to a certain degree the direct expression of the severity of the disease.

But, in a peculiar misjudging of the conceptions of cause and effect, and in far-reaching yielding to the modern trend of diagnosis which does not strive for a recognition of the connection of the manifestations, but is satisfied with a catchword, to-day cases are designated as diphtheria in which bacilli are present without disturbance of tissue; and thus, as stated before, the hypothetical generators are confused with the true cause,

and the cause with the effect—*i.e.*, the irritation with the disease.

It would be quite as correct to call a plum affected because fungi form a delicate whitish cover on the surface, to speak of inflammation of the lungs because the mouth contains pneumococci, or to speak of wounds because projectiles fly about. As a matter of fact, the plum does not become a medium for fungi until its face skin is destroyed or its nutrition greatly impaired, and the pulmonary tissue can not be called a brooding-place of pneumococci until its power of resistance is injured (*e.g.*, by refrigeration), and wound disease, or trauma, is not present until a bullet has entered the body.

Unquestionably nothing is more characteristic of the customary distortion and misconception of facts and their displacement by catchwords than this modern conception of the significance of microbes, identified as they are with the conception of disease, because the coincidence of two phenomena is erroneously placed on a par with causal connection.

We have never encountered this confusion of conception more strikingly than in the following sentence, taken from the cholera report of a prominent political paper: "Six inmates of the hospital had, or still have, Asiatic cholera, while none of them was or is sick." The explanation of this paradoxical statement is found only in the following concluding sentence, which we also render in its original style: "Namely, the physicians demonstrated in these persons the presence of the comma bacillus, which they are still possessed of, without, however, their suffering even from diarrhea; and for this reason they are as yet not discharged from the hospital,

altho they urgently request that this be done because they insist that they are not sick at all.''

However, this confusion of views, which places the possible cause of the recognition of the disease proper—hence, the (hypothetical) cause—on a par with all its consequences, also explains to the layman why the curative action of a new method and the extraordinary efficacy of our modes of disinfection and repression are so very frequently spoken of. Individuals who present no other abnormal manifestations but the comma bacillus may be readily cured, since they are not affected at all (by cholera), and naturally the restriction and extermination of the germs of cholera is easy if only comma bacilli, but not the conditions for the outbreak of an epidemic, are present. By the same token which identifies the comma bacillus with cholera, a candle burning in a room might be called a conflagration. A conflagration is not present until the flame has been offered an opportunity of operating upon combustible material; hence, combustibility is the main condition for conflagration, as predisposition is the basis of disease. The comma bacillus is unessential and insignificant in comparison to the pathogenic influences which create the predisposition, and it is not even demonstrated, in our opinion, that it is one of the most essential causes of the disease—*i. e.*, capable of calling forth the chain of phenomena which we call cholera.

If, in the same manner, every case in which diphtheria bacilli are found is designated as diphtheria; if, therefore, the still inactive (and hypothetical) irritation is thought of as already effective, then naturally the new treatment of diphtheria has by far the advantage of the old, because it *wrongfully* and in full claims the favorable

chances of the course of the doubtful cases which, as a rule, prove to be simple inflammations of the tonsils or of the throat.

This is the reason why its brilliant results—which, besides, are obtained only from a very small numerical material and in a very brief period of time—are apparent ones only; they depend, according to our view, as yet merely upon the *arbitrary handling of statistics*, quite apart from the fact that *local and general fluctuations of mortality*, so frequently shown by endemics and epidemics, may give rise to errors even of those who investigate skeptically.

Every other form of treatment of diphtheria will show favorable results if its efficacy is made subject to the condition that it is employed on the first day of the disease—*i.e.*, therefore, in cases in which, according to present clinical conceptions, the diagnosis between diphtheria and simple inflammation of the throat is quite impossible.

There is never any doubt in my mind that these explanations, which are intended to elucidate the uncertainty of the foundations and of the results so far achieved of an incisive method in which the interest of mankind has been aroused, and to be an admonition to calm, sober observation, will, for the present, not create a deep impression. However, they were not written to prevent those who consider the saying, “Nothing like trying,” their guiding principle, from the careful testing of the method on the most costly material (man), but they are intended merely to point out to turbulent enthusiasts the difficulty of tests and the long period of time required by the latter. Our discussions, furthermore, are meant to show how wrong it is to assign a leading part to humanity in affairs which are decided not by the heart, but by the intellect and by calm observation.

If the healing method, on account of which the minds of men are agitated, has but the most limited justification, success will become manifest also in those cases which in the quiet course of events form material of calmest objective observation. But the results will be falsified and comparison with other methods becomes impossible if cases are brought to treatment which, under normal conditions, would never have formed the basis for statistics. Before venturing an opinion concerning the effect of protection by inoculation, it is essential, first, to know the laws of infection of certain localities or of a city—*i. e.*, to know how often *one* case of disease in a family or in a dwelling is *followed by others* within a comparatively brief period of time.

Properly to measure the curative value of a method the statistics of hospitals must not be compared forthwith, particularly not when the number of those is greatly multiplied who are admitted merely for the purpose of a special treatment, and who otherwise would have stayed away from the hospital. This case obtains here. Since there are always persons who believe that humanity should be called upon only for valuable and safe achievements and for noble aims, then a method, the furtherance of which is so urgently recommended to mankind, must at the start be sure of the nimbus of a panacea and of the quality of being free from danger, and it can not fail, therefore, that suitable and unsuitable individuals crowd to be inoculated, as they at one time did for injection with tuberculin.

However, another evil must result from the combination of humanity and curative serum—namely, the higher prices of the remedy. The enormous demand for the preparation will, above all, serve to keep the price at a

considerable height for some time to come, especially since the charity of mankind is readily at the disposal of all.

I wonder whether the charitable minds who, in their enthusiasm, already saw the great enemy of child-life destroyed by their generosity, ever thought of it that their contributions might be destined to mature entirely different results than the saving of sick children? What loss will be suffered by the readiness of mankind to sacrifice, and by the valuation of medical science of the present day, if it should turn out that the appeal to humanity was made in the wrong place and prematurely?

The sums spent so far would have been sufficient to *promote true hygiene* in many families—*i.e.*, to improve the conditions of life and of nutrition, and to create favorable conditions of many a weak organism. The expenditures for high-priced inoculations have tended only to do homage to a passing whim of scientific fashion, possibly at the expense of the organisms of those that were inoculated, and at the cost of the confidence in scientific theories.

XXII

OROTHERAPY AND STATISTICS

I

The Foundations of Scientific Medical Statistics and the Changing of Systematic (Diagnostic) Views

No. 8 of the *Wiener med. Presse* of 1896 contains a statistical note on the mortality from diphtheria in the Paris hospitals¹ during the years 1880–1895, inclusive, which closes with the proud words: “The mortality from diphtheria in Paris has decreased by two-thirds since the general introduction of orotherapy.”

This communication appears to be calculated to arouse special interest, since apparently it most strikingly expresses the success of the new therapy. It is true, this deduction is weakened for the skeptic by the highly

¹ Average from 1880–1889, 1,840; 1890, 1,608; 1891, 1,361; 1892, 1,403; 1893, 1,266; 1894, 1,009; 1895, 435. Kossel (*Deutsche med. Wochenschrift*, 1896, No. 22) gives figures which differ but slightly from the above as to the mortality from diphtheria in Paris. Since the point in question here is only the significance of figures as members of a (declining) series, and since the curves of hospitals in their general character—*i.e.*, in rise and fall (of course, not regarding details) are usually very similar to those of the city in question, the significance of these figures is not altered by their origin. The figures, according to Kossel (respectively according to the publications of the Imperial Board of Health), are, for 1888, 1,718; for 1889, 1,706. Since the figures for the years 1886 and 1887 amount to only 1,565, respectively 1,524, it follows, provided the above average from 1880 to 1889 (1,840) is correct, that the mortality figures from 1880 to 1885 must be very high, so that the character of the series would become still more potent.

diplomatic supplement that *since* (not *in consequence of*) the general introduction of the orotherapy the mortality from diphtheria had diminished by two-thirds; however, this restriction applies only to particular skeptics, not to the superficial reader accustomed to bring data given to him simultaneously into a relation of interdependency. Even if it could be assumed that the author wished to utilize the phase of orotherapy merely as an historical event to determine the beginning of a new era, and not to represent the new method directly as the *cause* of the surprisingly favorable result, such a statement must not pass unchallenged, since experience teaches that many readers and investigators interpret the wording differently, and would construe a causal relation between treatment and decrease of mortality,¹ even in those instances in which it should be proven, above all, that it is not a question of a mere coincidence regarding time, perhaps as would the occurrence of a comet coincide with great revolutions in the history of nations.

It can not be too strongly emphasized that figures, even tho they may appear to point in but one direction, still require criticism, since the brutality of numbers, the insuperable demonstrative power of events determined by figures, does not depend upon numbers as such (the final result arrived at in some manner), but upon the assumption that the result has been obtained by irrefutable calculations from unassailable premises.

Statistical proofs are always more difficult than is generally supposed, since it is not a question of a simple comparison, respectively grouping, of results, of a comparison of figures (homologous quantities), but, above

¹ As a matter of fact, Kossel (*l. c.*) supplements the reproduction of these statistics with the words: "This table probably does not require a commentary."

all, of critical utilization and sifting of the material represented by a number—hence, of the real determination of fundamental quantities handled in practise. The neglect of these principles gives rise to the disregard of statistical results prevalent with many, which is usually founded upon the assertion that everything may be proven by statistics. But this reproach is justified only in those cases in which the events before and after a certain occurrence are compared without criticism; hence, in which the chronological sequence is looked upon as a causal relation, as it were, or upon the figures in themselves as values, respectively denominated quantities—as qualities instead of quantities—*i.e.*, it is omitted to examine the factors of the account carefully in regard to their value for the balance-sheet. But the individual figure (of a city or a village, of a county or of a state) for this balance-sheet is a complicated factor, requiring critical valuation before figuring as a sum to be included in the total.

Mortality statistics, therefore, quite correctly make distinctions regarding the occupation of the patients, the parts of the city, and especially regarding age; for it is obvious that, to judge the social or sanitary conditions (of a district), there exists a great deal of difference whether the mortality is due principally to the succumbing of the aged, or of nurslings, or of persons of middle age. It is absolutely impossible to draw any conclusions regarding a particular impairment of the general sanitary conditions from the fact that at one time two, at another time three, persons *pro mille* of the population have died (hence, that the mortality had increased at the enormous rate of 50 per cent.), since a great mortality among children and among the aged depends upon

entirely different factors, and is of an essentially different social, respectively natural, significance than that of strata and ages representing the true type of a people and its strength in the struggle for existence. We believe, for instance, that the mortality among children bears a certain relation to the number of births—*i.e.*, a large mortality of children is frequently nothing but a direct consequence of great fecundity of marriages, as from trees containing the greatest numbers of blossoms usually a relatively large percentage of the fruit drops off before becoming ripe.

Paradoxical as it may sound, the physical conditions of a population whose adult members are very strong throughout, may, even with a relatively great mortality, be designated as better than those of less vigorous population whose mortality is small only in the class of small children. If in a certain district relatively many weak children die during the first years of life, or if the number of the aged is relatively small, hence if the average age of the individual—representing three generations—becomes somewhat more unfavorable, still the result, the general standard of the health of the people, may, nevertheless, be more satisfactory than in other places in which many weak children remain alive and develop into a generation of middle age capable of but little resistance.

There can be no question that a slightly smaller number but a good development of the fruit permits of an inference as to better constitution and nutritive conditions of the tree—in this instance representing humanity—than more numerous but, in great part, fruit of inferior value. Of course, it does not follow that, because one certain age appears to be especially endangered, we should with particular attention search for the causes of this condition and look for means to relieve the same. But a relatively high mortality of very small children admits of a direct conclusion as to the health and resistibility of the people as little as the dropping off of a number of blossoms allows of an inference as to the quantity and quality of the harvest from a tree. Besides, it is

obvious that even a nation with a relatively high mortality of children may still increase more rapidly than one with a lesser absolute and relative mortality; for it depends entirely upon the surplus of births over deaths whether or not the population increases. If in one nation X children die per one thousand, and in another nation $\frac{X}{2}$, the population of the former, *ceteris paribus*, increases relatively by twice the amount if in the former $2X$, in the latter only X , children are born *pro mille*.

This overrating of the ease of statistical proofs harbors a great danger, because weapons acquired in such a manner may be very apt to turn against their bearers. If we consider ourselves entitled to stamp time relations forthwith as causal ones, and especially to regard prophylactic or therapeutic measures coinciding with a favorable change of the morbidity and mortality at once as the causes of these phenomena (in short, consider such proofs as scientifically unassailable and as sufficient at once to proclaim our therapy as omnipotent), then we can not very well raise objections if, upon the basis of similar reliable (!) foundations, an increase in the number of affections occurring from a certain period of time on would be traced to any non-essential event which, however, in the opinion of the laity, coincides conspicuously with certain remarkable happenings, or even to the deleterious effects of our therapy. And yet such inferences should be prevented in the interest of science as well as in that of justice. Any one who at once ascribes every decline of the morbidity and mortality curves to medical or hygienic art must not complain if subsequently a rise of the curve would be laid at the door of medical mistakes and sins of omission; for instance, if the sanitary authorities were to be blamed for a remarkable increase of diphtheria within a certain period of time.

If we boast that cholera was kept at a distance *only* by our energetic measures of disinfection and control, we would apparently be justified, in view of the enormous increase of diphtheria in Berlin, in pointing out that these allegedly so efficacious measures might possibly answer their purpose in cholera, but that they are entirely insufficient—yes, possibly even harmful—to combat *endemic* infectious diseases, especially diphtheria. Such an inference would naturally and justly at once be refuted by the adherents of the view that we have constituted the course of diphtheria to be greatly more favorable *solely* by *our* interference, altho they do not have any objections to the application of the inference *post hoc, ergo propter hoc* so far as their own curative cooperation is concerned; for they utilize the above-quoted statistics (and every other in their favor) in the sense referred to. They do not investigate the material for the proof, but unhesitatingly they regard a coincidence as to time as a proof of the causal connection, simply because success is the point in question.

The proof that the decrease must be ascribed to a certain factor, to the *new method of treatment*, and not to any other that is peculiar of the year 1895, and which possibly might have been foreseen, is furnished to him who looks for truth and does not take everything he finds to be the truth, only after all other possibilities for the development of an extremely favorable mortality figure have been excluded by a serious scientific investigation. It is true, the investigator, in constant belief in the possibility of reaching a high goal, must collect facts and severely criticize those he has collected, but he should not immediately believe in the infallibility of his conclusions when the facts appear for a short period to lie in the direction of his aim.

Therapeutic statistics compiled in a scientific sense must be based—as has been proclaimed innumerable times—upon *identical* material; they must not arbitrarily

change the conditions of the demonstration (the material) or ignore a change of important factors. However, the statistics of fanatics and enthusiasts never consider these principles. Preferably they utilize *brief* periods (months, single years); they employ with predilection the treacherous criterion of the relation between cases of disease and recovery (recovery quotient), instead of making use of the sure, absolute figures of mortality statistics—subject, also, it is true, to a critical exegesis; they operate with other definitions—*i.e.*, they employ preferably or exclusively diagnostic criteria which were not determining formerly, and thus exclude, with particular scientific thoroughness, all unsuitable cases until it is found that properly, upon the application of a new method, deaths should no longer occur at all. (That they still do occur is always the fault, according to the opinion of the adherents of the new therapeutic gospel, only of unfortunate external conditions—not to be laid at the door of the *method*—of certain complications which, it is true, the former unsuccessful therapists were also compelled to combat, or the impossibility of employing the cure-all method in time—an excuse which the adherents of the old methods certainly dare not bring to bear.) This method of dividing light and shade unevenly has been repeated innumerable times in the history of medicine, and it never loses its impression upon believing minds who can not or will not understand that most striking new results may be readily obtained even by the mere juggling-trick of a new scientific definition. Only the intelligent observer, knowing that nature does not advance by bounds and leaps, will be fully aware that necessarily in all cases in which suddenly the sum total of all prevailing views

appears to have been overthrown, a recoinage must have taken place of values which so far constituted the total result, an obscuring, as it were, of hitherto prevailing items of the balance-sheet.

We shall later on refer to the first point: the sources of error arising from the utilization of periods that are too short or are arbitrarily chosen; the other points will presently be briefly discussed. Here let us remark that, in the sense of finding a (biological) law which therapeutic deductions should or mean to be, every period of time not embracing several decades must in reality be considered too short.

One year is but a brief measure of time for the theory of epidemics, for the judging of the undulations in the history of mankind manifested in the invasions of devastating diseases, but, above all, for the determination of the value of an influence created by the hand of man, since in these cases the crests and the depths of the waves embrace lustra and decades, since epidemics, like the invasions of locusts, of caterpillars, of the development of May bugs (*melolontha vulgaris*), present inexplicable periods of acme and remission.

Altho every one knows that small figures prove absolutely nothing, altho every one is familiar with the law of large numbers, still small figures are preferably employed, and even many of those who consciously utilize only large figures, hence believe to take this law into account, are in error regarding its range, since not the large figures in themselves, but the circumstances under which they were obtained, are of importance. The value of large figures depends, above all, upon the factor of time—*i. e.*, upon the length of time during which the details were collected, upon the duration of the series of

observation; for five hundred cases collected and analyzed in ten years under homologueous conditions by the same observer are of greater significance than five hundred cases observed during one month in the same place or even gathered from everywhere, since in the former instance, quite apart from the more precise weighing of values, probably all possibilites were active by which figures might be influenced, hence mistakes have become adjusted, whereas it is most probable in the second instance that figures obtained under the influence of one and the same (one-sided) direction of development are subject to the faults of small series—*i.e.*, they do not sufficiently exclude accidents. The reliability of conclusions is in an inverse ratio to the time of observation—*i.e.*, the conclusions remain uncertain even if the brief observation extends over large territories and furnishes large figures.

A special cause of error is furnished also by a comparison of the figures representing the relation between the cases of affection and those of death, respectively the proportion between those that had recovered and those that were affected—a determination which, at the first glance, owing to its simplicity, appears to be sufficient to furnish the only correct criterion for decision. However, the apparent paradoxia of the dictum that the very determination of such percentage relations is the source of error will be amply verified if the uncertainty and the inconstancy of the principles governing diagnosis are considered, hence the uncertainty of inductive foundations; for definition, respectively conception, is, after all, unfortunately, the creator and the measure of all things, the foundation of all attempts at legitimately regulating all phenomena.

Naturally, a comparison of two periods (or series of events) may lay claim to the designation "scientific" only upon the presumption of the trustworthiness of the foundations, because then every one is in a position to test the correctness of the conclusions upon the material on hand. The individual cases of statistics, therefore, must represent the same quantities, respectively units; but this they are capable of doing only when the same criteria govern the definition (in medical subjects the diagnosis). Therefore, the reliability of the material (for comparison) is in a direct relation to the simplicity of its acquisition—*i.e.*, the larger the number of possibilities for definition, the more heterogeneous the material may become, in spite of its being obtained inductively (by exact observation), for the very reason of its classification on the basis of a subjective opinion (diagnosis), the more unreliable will be the comparison on behalf of statistical conclusions.

If, for the purpose of scientific investigation of new, especially therapeutic, factors, the number of those who recovered is in two series of observation (periods) to be compared with that of the persons who succumbed (*i.e.*, if the alteration of the quotient of those who recovered is to be determined in an unobjectionable manner), the presumption naturally obtains that the new view-points do not cause a change of material, that the same criteria serve to form the diagnosis, and that the classification of the cases is done on the basis of an identical definition. Any one who calls every inflammation of the throat a diphtheria will, of course—and this can not be too strongly emphasized—always have the most favorable number of recoveries, since one hundred cases of inflam-

mation of the throat include possibly only ten cases of true diphtheria.

For instance, if the average mortality of diphtheria in private practise, as I believe, amounts to 10 per cent.—at most, 20 per cent.—the latter physician will have one to two cases of death, or, since he has treated one hundred cases of diphtheria, expressed statistically, 98 per cent. to 99 per cent. of cures; another physician, who also has had one to two deaths, will have (since he makes the diagnosis of diphtheria only rarely, hence has treated ninety cases of ordinary inflammation of the throat and ten cases of true diphtheria) these cases of death in ten cases of diphtheria, and he will, therefore, show 10 per cent. to 20 per cent. mortality and only 80 per cent. to 90 per cent. of cures—*i.e.*, he lost, as is demonstrated with imperturbable logic by apparently impartial statistics, five times as many cases of diphtheria than did his colleague whose favorable results, to those who investigate thoroughly, are really due less to the art of therapy than to his method of diagnosis. If the second physician had lost four patients—which may happen quite readily—he would have, among one hundred patients, only two deaths more than his colleague (96 per cent. against 98 per cent. cures), which really is of not much account; but the mortality of his diphtheria patients would have been frightful, for it was as high as 40 per cent.

What, then, shall we think of comparisons undertaken with constant and complete change of the methodical view-points, as is so often the case in medicine, since a new therapy is usually the outcome of new systematic views. Does there exist any possibility at all of a scientific comparison of two periods if in the one instance only those cases are considered, the clinical pictures of which present distinct features known even to laymen (text-book cases or types), whereas in the other instance those cases are also counted as homogeneous in which even the most experienced physician is not able to form an opinion regarding the nature of the process—yes, not even

whether an infection is present at all? The glory is easily procured of having suppressed revolutions, or of having cured severe diseases, if every gathering of three persons is called a riot, and every feeling of discomfort a disease that might be classified in a category formed of typical cases—hence, is systematically defined.

He who at once administers a febrifuge in every rise of temperature will have entirely different views regarding the efficacy of antipyretics than a physician who satisfies himself that the temperature returns to normal in one day without any treatment in about 80 per cent. of the cases; any one who attempts to have every slight disorder cured by “incantations” will gradually become convinced of the significance of this curative method.

If a remedy is adjudged the special faculty of being the more efficacious the earlier it is employed, and if a particular innoxiousness is also attributed to it, then, naturally, it will be employed at the least provocation—*i.e.*, in cases in which the severity and character of the disease can not yet be determined—yes, sometimes not even whether an actual affection is really present. If an infallible and harmless remedy against cancer is recommended, very soon a great number of individuals, many more than really suffer from cancer, will make use of the remedy, since, besides those afflicted with cancer, imaginary patients and a number of others whose doubtful condition renders a diagnosis impossible even to the experienced physician, will eagerly take hold of the remedy. A further consequence will be that the lucky inventor of such a remedy will treat and cure an enormous number of cancer patients; for there is nothing to prevent him from assuming of all persons who employ the remedy that they suffer from the first—hence, not yet fully developed—forms of cancer. In other words: “Whereas, formerly ten cases of cancer figured in the statistics of a given place, of which, according to the diagnostic tendency of the physicians, between 60 per cent. and 100 per cent. died, now there will be fifty cases of the disease of which naturally only six to ten are fatal—*i.e.*, the mortality has gone down to 12-20 per

cent. Now, if a man of science is the discoverer of the method, then jubilation over the imposing curative result—the triumph of science—becomes general, and only the more skeptic and experienced portion of physicians, who for the time being would ascribe an especially favorable mortality in cancer (and other malignant affections) not to the efficacy of the remedy or method employed, but to the diagnosis, will not join the general jubilation, even at the risk of being accused of unscientific thoughts, of ignorance, and even of envy.

Hence, the modern form of diagnosis, naturally also that of diphtheria, contributes materially to these scientifically inadequate proofs, artificially obtained, of the value of a certain therapy—they might be called improvement of therapy by conceptive or calculative (diagnostic or statistic) methods—respectively to the gaining of especially favorable results upon an apparently unassailable statistical basis; for, as unquestionably every one who shows diphtheria bacilli, even without other serious manifestations, is at once recorded as a diphtheria patient, his recovery is credited to the account of curative serum, altho danger to the patient was possibly never present in the eyes of the expert, since not the presence of bacteria, but only the character and the intensity of all symptoms, respectively the abnormal forms of the reaction of the organism (of the tissues and organs) can furnish what we call disease (disturbance of the equilibrium of activity). Sick is not he in whom bacteria can be demonstrated in the cavity of the mouth or in other localities (for the number of bacteria is legion), but he who harbors within his cells, in his tissues, or in his blood, smallest organisms which essentially alter the economy of the body and permanently diminish activity.

Since, under the influence of bacteriological principles, the view-points for statistical judgment have materially shifted during recent times, it is irremissible to begin every criticism of the evidences furnished by the modern school with a general discussion of the principles and methods constituting the weapons in the contention, to examine, as it were, the present intrinsic value of the coins of scientific traffic. The silver currency of scientific truth emanating from the official mints of scientific values often shares the fate of the currency of the realm; the flag covers the goods of lesser value. The coin has a high quotation, but not a corresponding intrinsic value; it passes only so long as powerful protectors guarantee its value which otherwise is far less and sometimes imaginary.

But to test the current coin as to its true value we must not be determined by the external appearance and by the authority that puts it into circulation, satisfied with such values, but we must subject every contention to a careful test upon the touchstone of calm criticism and experience. Therefore, a special criticism of the apparently unassailable numerical statements, of the imposing columns of figures, is indispensable, and, therefore, we shall proceed to do so, in that we apply the previously obtained view-points to the judging of the value of the individual quantities—hence, endeavor to reduce, as it were, indefinite (ambiguous) figures to unambiguous (denominated) quantities.

The new therapy is in a very favorable position in this respect; for every case of doubtful diphtheria, the mildly abortive cases which are sure to recover, and also simple inflammations of the throat, may, early subjected to injection, be utilized as a proof of the efficacy of the

method, since the cure—at least, according to the logic of modern therapeutists—proves that the injection has destroyed the disease, even if bacilli may be demonstrated in the mouth or throat for weeks after. Such patients are cured and immune, altho they harbor specific microbes; but entirely healthy persons presenting the same condition are neither well nor immune until after they have been immunized by means of injections.

Of course, the cases in which the disease is aborted are fully demonstrative to the defenders of bacteriological diagnoses, even tho the disease were characterized as true diphtheria, merely by the demonstration of some few (specific) bacilli, for such cases are to the bacteriologist homogeneous with those of true diphtheria so soon as they present the connecting-link of systematic classification, the pathognomonic principle, the bacillus.

One-sided statistics are still further favored, in that no case with lethal termination, even if evident diphtheria is manifest according to clinical designation, must be charged to the account of failures so soon as the bacteriological examination shows the presence of different forms of microbes, inclusive or exclusive of diphtheria bacilli, since only cases of true diphtheria are qualified for the method, respectively are subject to the beneficent action of the serum. However, we doubt very much whether the cases of recovery are registered quite as scrupulously as the fatal ones, and whether the mixed forms or those which did not show the diphtheria bacillus are now rigorously excluded from the category of demonstrative cures, since they can not be influenced by the serum; statistics published thus far do not furnish any points in this respect. It appears, therefore, that the old form of diagnosis is sufficient in all cases of cure;

in cases with fatal termination, on the other hand, only those are considered valid which are classified as genuine by the most exact bacteriological investigation. Endeavors are also had to relieve the serum of the responsibility of cases that come to treatment too late, whereas failure in cases of diphtheria which in former times also were treated very late—possibly much later than now—was ruthlessly charged to the ineffective therapy of the past.

To be impartial, endeavors should be made at least to establish the success that was accomplished in former times in all cases of inflammation of the throat—immaterial of what nature—provided they were made subject to careful treatment on the first day. It will then at once be plain that every form of inflammation of the throat which is not treated until the third or fourth day runs a much severer course, because it represents a severe affection from the very beginning or because it was protracted. Nothing is ever heard of any of these considerations; the quotient of recovery of former years is simply compared with that of the years 1894 and 1895, of which the year 1894 is of not much account, since a general application of the serum can at best be spoken of only for the last three months. And this is claimed to establish the efficacy of the method beyond all doubts, altho attention has been repeatedly called to the fact—among others, by myself—that the number of those treated for diphtheria in hospitals is much larger than for many years past.

There can be no doubt, therefore, that, in the *bacterial diagnosis in absentia*, which is so much in vogue now, and which can not be too strongly condemned, the frequent deaths of the very dangerous scarlatinal diphtheria which in many places and, in my opinion, correctly so, were counted as diphtheria (as scarlatinal nephritis is counted as acute nephritis), and which were surely to a great deal responsible for the former high mortality, are now mostly classified separately as deaths from scarlatina, thus naturally again placing the effects of the serum in the best possible light.

II

Absolute Mortality and the Character of the Series—Significance of Undulations in the Realm of Epidemiology

For all these reasons, to judge the value of a remedy we prefer the figures of absolute mortality naturally, not to utilize the absolute figures at once for conclusions, as was believed could be done with ease at the hand of the above-mentioned Paris statistics, but because the absolute figures offer the most important foundations for forming an opinion. The absolute number of the cases of deaths represents the direct extent of damage sustained by the population by some form of disease, whereas the determination of the quotient of recovery introduces another view-point for judgment; hence, as all figures of ratios, it is subject to the possibility of a subjective construction and reinterpretation of the results.

It is true, the absolute mortality figures may be considered as equivalent members of full value of a series, of a group of events in constant relation to each other—in short, as the foundation of a scientific conclusion—only when the old premises for the definitions remain valid, and when only longer periods are compared. Neither must the (changing) character of the series be neglected in the periods to be compared, but endeavors must be made first to determine whether the aggregate of all the members, or some successive members, present special peculiarities, whether certain laws exist which, dependent upon the natural course of events, impair or even exclude an explanation in the sense of the newly formulated view-point, because events have previously

moved distinctly in a direction corresponding to the new influence.

For instance, if a business concern is improving or declining, and for years has yielded increasing or declining results, it would not be correct to regard a measure employed at any arbitrary moment, after the introduction of which the improvement or the decline becomes especially apparent, as the cause of events the direction of which was manifest to the experienced for a long time previous. Special care must be had if an apparently sudden change forces us, as it were, to construe causal relations between a synchronous event and the course of mortality; for such conclusions are very unreliable if the tendency to a change had been distinctly manifest in the nature of the series, or if the figures of a longer period move with conspicuous constancy above or below the average.

That seven fat years are usually followed by seven lean ones—*i.e.*, that the directions of development *change*—does not apply only to Egypt, and if the figures of any event, for instance, of the course of a certain disease for twenty or thirty years, are at command, it will not be difficult to determine the different, distinctly marked, periods of constant rises and declines of the curves and of the tolerably regular duration of the individual phases of an equal tendency. We shall find that a lustrum or a decade of equally high mortality is followed by several years of low death-rates, and that a low mortality is commonly succeeded by a high one. The undulation is distinct even in those cases in which the mortality, respectively morbidity, of a certain form at last becomes extraordinarily small; the curve rarely falls constantly, but it shows exacerbations—mountains and valleys.

These phenomena are naturally most distinctly pronounced in *endemic* diseases, for which about three decades might form a period, during which, of course, changes of onomatology

must be carefully considered; for cases which some thirty to forty years ago would have been designated throughout as typhoid fever, have subsequently with certainty been recognized and designated as meningitis, acute miliary tuberculosis, uremia (cryptogenetic), pyemia. Besides, the *genius epidemicus*, respectively the character of the disease, must be taken into account for *all* forms of the affection; for it is obvious that not *all* species of disease can *at the same time be equally deleterious—i.e.*, decimate mankind. According to my experience, there are periods in which the acute, and other periods in which the chronic, diseases more particularly decimate mankind; periods in which preferably nurslings or the aged succumb, and others in which adults or the senile are taken off; periods in which wound diseases, and others in which internal affections, prevail, not to mention wars, which change the conditions of morbidity and mortality for decades to come.¹

The figures of morbidity, respectively the quotient of recoveries, are quite unreliable for forming an opinion, since the result depends too much upon the principles determining the formulation of a diagnosis, and, besides, other reasons and proofs are decisive in the diagnosis during life than obtain in the statement of the cause of death, especially in that based upon necropsy results. Aside from the persons concerned as godfathers or originators of a therapeutic method (who in these cases, in spite of their desire to remain objective, can not, as parties, fully forego subjectivity), nobody has any interest in making artificial differences in cases of death; on the contrary, the physician concerned is, in the eyes of many laymen, at once exempt from all blame if he has sufficiently early given to the fatal disease a name which breathes disaster. That even the best medical treatment

¹ Wars also are probably the expression of a law unknown to us in the development of mankind, and their influence is quite as important to the medical statistician as that of epidemics or important social factors.

can not save a person suffering from acute miliary tuberculosis, blood-poisoning, or septic diphtheria, is more readily comprehended than the possibility of any one succumbing to a gastric fever or a mere angina. But so soon as the influence of a therapeutic method is to be judged statistically, the view-points of physicians and laymen are changed; for the cause of death in many individuals who succumbed to operation is given as cardiac asthenia or inflammation of the lungs, whereas the fatal termination should in reality be laid at the door of the operative interference, or, if the operation was performed too late, to the original disease.

The expert must become puzzled regarding the foundations of statistics when he notices that a remarkable increase of a certain affection is associated with an unexpectedly small mortality. For in cases in which an increase of the number of endemic diseases is actually to be attributed to natural influences, in which the point in question is the development of a true epidemic, the mortality, with very rare exceptions, generally rises quite considerably. But the conditions are usually reversed in cases in which fashion or other inessential influences participate materially in the size of the figure, and in which the denomination of the cases, respectively the manner of diagnosis, plays a determining part. Thus, according to our opinion, the marked increase of the cases of diphtheria during the last two years may possibly be due to another factor than to the natural course of events—namely, to the new form of diagnosis. At any rate, the assumption that we are dealing with a natural undulation in the current of the affections from diphtheria is not an entirely positive one; it will not be proved until after it has been determined that the

increase is not due to the principles of classification, or that the same criteria regarding rubrication are still in force at present.

Now, it would probably never do to ascribe the unquestioned increase of diphtheria patients in the hospitals of Berlin merely to external (non-essential) influences, such as the new laws regarding sick-funds, greater readiness of the public to apply to hospitals, etc., because these figures have also risen outside of the hospitals, which in part may also be due to the fear lest a case may be taken too lightly, thus keeping it from being disinfected or treated with serum. It is not impossible, therefore, that here, too, the method of diagnosis plays an essential part in formulating the figure of the affections; however, this can be decided only if it were possible to compare the figures of those treated in the hospitals for the various forms of inflammation of the throat during the years from 1880 to 1895 among each other and with the figures of diphtheria in the respective periods. The comparison would readily show, provided sufficient care is observed, whether the diagnosis of diphtheria is now made more frequently than formerly—in short, whether or not it is more in keeping with the modern tendencies than that of simple angina.

It is possible that for the Charité Hospital, for instance, a new factor, important for the compilation of the morbidity statistics of infectious diseases, has become active by the creation of the institution for infectious diseases.

Kossel (*Deutsche med. Wochenschrift*, 1896, No. 22), to prove the effect of the serum, utilizes the results of a period covering a number of years (from 1886 to 1896 inclusive), but he opposes the short era of the serum (in which he includes the year of 1894) to the other (eight, respectively nine) years. He gives the following four tables, to which we have added the average figures for periods of five and three years, in order to demonstrate the striking differences of the foundations for

therapeutic or causal consideration resulting from this distribution:

TABLE I

Admissions and Mortality of Diphtheria Patients in the Charité¹

YEAR	Admitted	Of these there died per annum					
		In periods of					
		5	3	4	years		
1889	116	51					
Jan. 1, 1887, to Mch. 31, 1888	157	86					68
Apr. 1, 1888, to Mch. 31, 1889	103	92					
1890-90	107	87	80	88	79		
1890-91	140	146					82
1891-92	104	65					
1892-93	152	83		77	77		
1893-94	168	77					
1894-95	306	41	61	52	40		60 (!)
1895-96	265	285 (!)	40				

TABLE II

Admission and Mortality of Diphtheria Patients in all Hospitals of Berlin¹

YEAR	Admitted	Of whom died	In annual average per			
			Lustrum	Triennium		
1885	1928	789				
1886	1738	609		609		665
1887	1636	598				
1888	1446	523	599	565	681	
1889	1623	573				608
1890	1792	625				
1891	1764	623		718		
1892	2074	837				
1893	2450	951	789 (!)		789 (!)	
1894	2690	801		745 (!)		768 (!)
1895	3061	484	642 (!)			

¹ The brackets show the periods to which the average refers.

TABLE III

Reported Cases and Deaths of Diphtheria Patients in Berlin

YEAR	Reported	DEATHS				
			Lustrum per annum	Trienn. per annum	Quadriennium per annum	
1886	6968	1632	} 1406	} 1266	} 1356	} 1512
1887	5438	1392				
1888	4190	1195				
1889	4320	1210				
1890	4586	1601				
1891	3504	1106	} 1298	} 1350	} 1421	} 1278
1892	3683	1342				
1893	4315	1637				
1894	5220	1416				
1895	6106	987				
			} 1201	} 1347 (!)	} 1201	} 1345 (!)

TABLE IV

Deaths from Diphtheria in German Cities of more than
15,000 Inhabitants

YEAR	Absolute number of deaths		Of 100,000 inhabitants there died of diphtheria per annum in the pe- riod encompassed by brackets						
		Lustrum per year	Triennium per year						
1886	12,211	} 11,431	} 11,010	} 11,310	} 106	} 108	} 104	} 109	} 115
1887	10,970								
1888	10,142								
1889	11,919								
1890	11,915								
1891	10,484	} 12,161 (!)	} 11,588	} 12,653 (!)	} 98	} 98	} 95	} 104	} 98
1892	12,365								
1893	16,557								
1894	13,790								
1895	7,611								
					} 77		} 95(!)	} 77	} 95(!)

Doubts must arise in the mind of every unbiased statistician whether years which present such a difference of figures, as do the years 1894 to 1896 of the Charité

statistics, should at all be compared with each other, either in a favorable or in an unfavorable respect. Here it is necessary, above all, to wait for the results of subsequent years; for even comparison of the figures of the Charité Hospital with those of all other hospitals of Berlin furnishes a perplexing conclusion which was not drawn by Kossel—namely, that to the (yearly) figure of the eight years' average—*i.e.*, 688 deaths—corresponds the figure 642 in the era of the serum of scarcely two years' duration. The diminution of the mortality is minimal, therefore; it amounts to about 6 per cent. (at the Charité 50 per cent.), and the respective death-rate is more unfavorable than that of the lustrum 1886 to 1890. On the other hand, the decrease of the total mortality of Berlin, when comparing the biennium with eight previous years, amounts to about 13 per cent., it is true; but, nevertheless, the mortality has not become less than in some of the previous biannual periods (for instance, the years 1888 and 1889), which were still under the rule of an allegedly inefficacious therapy. Such variations should be sufficient to perplex even the most eager statistician, and caution him to be careful regarding conclusions or to wait before reporting results. Since, further, it may be assumed that serum was exclusively employed in the hospitals, whereas in the city proper many cases were probably treated differently (and too *late*), it is more than likely that other factors than the serum must be held responsible for the small mortality among those who were affected in the city.

How is it possible to determine the influence of the new therapy unobjectionably by the consideration of only two years, or what is at all to be compared if two

periods of five years each present such absolutely opposite conditions of the undulations of mortality as did those of the last decade, if the morbidity from 1891 to 1895, inclusive, rose from 3,504 to 6,106 patients, whereas from 1886 to 1890, inclusive, it declined from 6,968 to 4,190? It is impossible, if comparisons are at all to be made, that such a comparison should be utilized to judge the therapeutic influences; for then the conclusion would be reached that the treatment of the year 1886, during which only 1,632 patients died of 6,968 that were affected, was incomparably better than in 1890, when, of 4,586 patients, 1,601 died. Since in the two years 24 per cent. (respectively, 35 per cent.) died, it follows that the therapeutic measures had become about 50 per cent. less effective during the last-named year. Since, furthermore, mortality in the year 1893 amounted to 38 per cent., and was still 27 per cent. in the year 1894, during which the serum was allegedly used extensively and with good success, we can not really speak of an influence of the serum at this period, since mortality had once before (1886) been brought down to 24 per cent. Whenever such extensive undulations exist, comparisons of single years, or even of short periods (from two to three years), are not possible at all, since conditions of a different general character, of an entirely different tendency of reaction and predisposition, are too apt to be compared with each other.

For instance, if the figures of all the Berlin hospitals (Kossel, *l. c.*, Table II.) for two lustra each are opposed to each other—hence, the years from 1886 to 1890, inclusive, and 1891 to 1895—the differences would become still more evident if 1885 would be included, as the real flood-tide of this period for Berlin still occurred during

that year—we obtain, with 2,998 respectively 3,787 deaths in the first lustrum, an average mortality of 599 (considering six years, it would be 631), for the second lustrum, with 3,696 deaths, an average mortality of 739 per year—*i.e.*, a considerable difference to the disadvantage of the last period—so that the serum must prove a great deal more useful to reach the mortality of the period without serum. Likewise is the mortality of the last period for German cities of 15,000 inhabitants and above (Table IV.) still unfavorable. The figures are: For 1886 to 1890, 57,156 (per year, 11.431), and for 1891 to 1895, inclusive, 60,807 (per year, 12.161); and even the improvement for the years 1895 respectively 1894 is only apparently so very prominent, because 1893 had an immensely large mortality which, in the natural course of events, was bound to be followed by a considerable decrease. Whereas, namely, the *average mortality* of 1886 to 1892, inclusive, amounted to 11.429, that of the year 1893 was 16.557—hence, about 50 per cent. higher, and still over 30 per cent. above that of the preceding year (already conspicuous by a more marked relative mortality), a fact which more than explains the decrease in 1894. Even if we consider periods of THREE years, the death-rates for 1887 to 1889, inclusive, are 33.031, for 1890 to 1892, inclusive, 34.764, and for 1893 to 1895, inclusive, 37.958; hence, in spite of the alleged action of the serum, the greatest mortality of a triennium.

Besides, the examination of the same Table IV. (diphtheria mortality in cities of 15,000 inhabitants and above) evolves the remarkable fact that the absolute number of deaths has risen considerably, whereas the death-rate, calculated for 100,000 inhabitants, has materially decreased—namely, the

average for 1886-1890 for 100,000 inhabitants is 108; for 1890-1895, 93; so that the absolute number of deaths (see above) has increased by about 6.3 per cent., and the mortality per 100,000 inhabitants has decreased by about 14 per cent. This difference is quite as conspicuous if we omit the last year; for then the absolute figure, as against the first lustrum, has risen from 11,431 to 13,299 (hence, by 16 per cent.), whereas the mortality per 100,000 inhabitants has diminished by more than 4 per cent.¹ This fact also is probably a proof that traps are concealed in all statistics, and that even the statistics for 100,000 inhabitants offer considerable differences regarding their explanation as against that of the absolute number of deaths. At any rate, the ratio that results in this instance proves that the population of the large cities has increased more rapidly than the mortality of diphtheria, and that every reduction of the absolute figures to another scale necessitates new researches to arrive at conclusions. It is not possible at at once to deduce from an improvement of the death-rate for 100,000 inhabitants that the therapy or any other artificial factor must have been active in the present sense. It is probable that the increase of the city population was due to individuals who are less inclined to become affected by diphtheria—*i. e.*, the population has probably increased principally by the addition of adults, unless still other factors are active, which can not at once be determined.

How little determining the handling of statistics is in the hands of the adherents of orotherapy, of how little importance are some few local occurrences, is also proven by the following tables of diphtheria morbidity and mortality—comprehensible even without any comment

¹ Calculated for periods of three years, the figures per 100,000 for the first period ('87-'89) are 311; for the second ('90-'92), 286; for the third ('93-'95), 284; the absolute figures, 11,010, 11,588, and 12,652—hence, absolutely incongruent, since the first figures form a rising series, the second ones, a declining series. Besides, a distinct approachment of the figures per 100,000 evinces that the prevailing form of the formation of mortality figures is about nearing a change, respectively comes to a standstill.

—in Breslau, for which I am indebted to the kindness of Dr. Neefe, director of the Statistical Bureau :

Cases and Deaths from Diphtheria in the City of Breslau

YEAR	Patients	Deaths	Average for	
			3 years	5 years
1880	175	68		
1881	312	97		
1882	381	163	} 471	} 794
1883	496	211		
1884	551	161		
1885	502	162	} 550	} 794
1886	752	227		
1887	1635	443		
1888	1675	443	} 1234	} 1783
1889	1434	348		
1890	1171	322		
1891	820	262	} 794	} 1320
1892	779	210		
1893	1016	355		
1894	965	280	} 848	} 1320
1895	1072	213		

Deaths in the Allerheiligen Hospital in Breslau¹

YEAR	Deaths	Average for	
		3 years	5 years
1880	10		
1881	14		
1882	41	} 130	} 253
1883	75		
1884	63		
1885	60	} 191	} 179
1886	68		
1887	111		
1888	115	} 334	} 513
1889	108		
1890	111		
1891	85	} 266	} 418
1892	70		
1893	116		
1894	76	} 258	} 418
1895	66		

This table illustrates plainly how careful we must be with conclusions from analogy, for the results show nothing of the effect of the serum which was certainly considerably used in 1895. But it demonstrates how difficult it is to compare short periods and different

¹ We wish to state that here only the number of cases treated in the Allerheiligen Hospital is reported, because the cases reported by the remaining hospitals, even in the last lustrum, do not amount to more than 10 per cent.—hence, do not influence the result in any noticeable manner. It should be stated, further, regarding the increase in the number of inhabitants, that an increase per lustrum of about 10 per cent. must be assumed—hence, about 2 per cent. per year—so that the figures as given for the third lustrum, if it is desired to make this correction, are by the corresponding percentages too high. Therefore, as Breslau counted about one-third more inhabitants in 1895 than it did in 1880, the number of deaths for 1895 should, *ceteris paribus*, be reduced for exact comparison—i.e., not 213 should be taken, but about 141, and for the preceding year 196, etc.; therefore, high death-rates which surpass the most favorable mortality (for 1880) by more than double, respectively three times.

localities, since the period 1886-1890, inclusive, presents relatively enormous mortality figures, and the mortality of Breslau during the last two lustra shows the converse of the proportion of average mortality of other large cities (Table IV. of Kossel), which presents an increase (of 19.20) in the last lustrum, whereas the greatest mortality for Breslau existed in the last but one lustrum (proportion of the two lustra, about 10.7). It demonstrates, finally, that diphtheria in Breslau took an exceptionally favorable course in the years 1881-1883. The table proves, further, that the year 1893 was the worst of the last lustrum, and that—hence, according to former experiences—a decrease in the number of deaths during the subsequent years could be prognosticated with a certain degree of probability—*i.e.*, figures could be looked for which better corresponded to the average of the other years of the lustrum.

How absurd it is to utilize any brief periods as a proof of the significance of therapeutic measures is shown by a glance at the table of deaths from diphtheria in the Allerheiligen Hospital. From 1888 to 1892, when this division was under my direction, the mortality had gradually decreased by 50 per cent., whereas it had quite as constantly risen during the preceding years. Subsequently, in 1893, it very nearly doubled. Can any one seriously believe that therapeutic influences were determining here? Those who examine the statistics of fifteen years without being prejudiced must assume that some factors are at work which are not known to us, and which are as little dependent upon our measures as the changes of the weather. It is true, better conditions appear to become prevalent again also for Breslau; let it be hoped that the mortality will now approach that of the favorable lustrum from 1880 to 1885. The principal action of the serum will, therefore, probably occur for this city during the next two years, whereas, in Berlin and in the western part of the country, in which districts the source of the epidemic was an

entirely different one, according to the statistics, it had taken place during the preceding years. Hence, such statistics must be utilized only if a *long* series is known which shows a certain character; only then will it be noted what accidents obtain in determining the results of brief periods.

Nearly all these points have often been discussed; however, these objections to the current method of utilization of figures have created but little impression, since impatience urges rapid demonstration, since the criticism of statistics is not every one's forte, and since two bare numbers represent, in the eyes of the majority, so striking a proof that a whole series of most serious objections to their significance, dictated by experience, are not able to disprove it.

It has probably become clear from these discussions that we consider the above-mentioned mortality statistics of Paris so particularly important, because they furnish absolute figures of death-rates for a long period, and they shed a prominent light upon a source of error which as yet has not been sufficiently taken into account—namely, the errors resulting from the extreme shortness of the periods compared, which very frequently have rendered the most careful calculations worthless.

If simply the last two years of the statistics, the terminal members of the series, are compared with the first ones, as was already done, then, it is true, the conclusion can not be avoided that the mortality has greatly decreased since the use of the serum. But, if we were to infer that it had been decreased by the serum, we would judge very superficially, because we omit to investigate the general character of the former periods, and to determine whether a distinct upward or downward tendency of the figures was prevalent.

If, namely, in the statistics that concern us here, we consider the years previous to 1895, we shall see that—except the year 1892, which equalizes, as it were, the markedly favorable course of the affections in 1891, thus preserving the average difference of the arithmetical series—mortality moves in such a distinctly descending series as may well be imagined. The mortality which, until 1889, still averaged 1,840, was only 1,009 in 1894—hence, had decreased by about 45 per cent. in comparison to the maximum; so that this fact would lead us to infer a special efficacy of our methods during the two last lustra, provided such an inference appears at all justified for an epidemiologist who must consider the laws of periods and not the isolated facts of brief spaces of time. If, further, the conspicuous decrease from 1893 to 1894 is considered—it amounts to double the decrease from 1892 to 1893—it would have been possible to prognosticate for the year 1895, simply from the knowledge of the series, a diminution of the cases of death by 514 (twice 257); of course, providing the persistence of the same conditions, and provided that no unforeseen events occurred which abolish *all* human deductions. The decrease of the deaths by 514 would have resulted in a mortality of 495 cases in 1895, whereas in reality only 435 deaths occurred—hence, even a few less. This difference in itself is insignificant; nor is it of great importance, in view of a declining series as distinct as the one here determined.

If through several members a series has acquired a certain constancy in one or the other direction, then the probability is at hand that the character will remain the same also in the following members, as within certain limits is the case also regarding the persistence of equal conditions of the weather.

After it has rained for eight days in succession, the probability is quite great that it may rain two days more, but it would be wrong to extend this proposition to longer periods; on the contrary, it is much more probable that fine weather will follow after the rain has persisted for fourteen days. But, naturally, there exists no absolute certainty as to the validity of such assumptions in any domain, since the great *distinct* undulations, the foundations of the phenomena which we look upon as following a certain law, are possibly secular; they represent the equalization of the small oscillations which we, in great near-sightedness, are fain to regard as the expression of *biological laws*. In the realm of medicine the same constellation may possibly not develop until after three to four decades, if for no other reason than because the consecutive generations are not homogeneous, but correspond to systems of undulations of different extent and form, as is expressed in the manner of the vital manifestations, respectively in the faculty of reaction, in the physical and mental domains (plethoric, anemic, nervous constitutions as the average types, special forms of the trend of thought that are best gathered from the catchwords of that particular era, etc.)

The difficulty of formulating laws of morbidity and mortality for individual groups of disease which, after all, correspond to an artificial system, is all the greater because it may be possible that quite different conditions may prevail at the same time in different sections, country and city, province, state, continent, as also in the various races and nations, in consequence of external or internal, economic or other influences, so that in one country the inhabitants of which are not yet predisposed to disease of a given form, any protective measure is effective, whereas the inhabitants of another country succumb, no matter what defensive arrangements are made to ward off disease. (Compare the course of cholera in the last decade in the various states of Europe.) In the same manner it may be observed that measures are effect-

ive in one state which, in another country and at another period, prove themselves to be entirely inefficacious, so that absolutely contradictory results are reached in comparing long periods of time (hence, one learns to recognize the doubtful value of such measures), whereas, on the basis of the material of too short a period, we usually become convinced that a nation or a district has remained free from the disaster that affected another part of the world *solely* by the institution of certain protective measures.

Rarely only will the undulation of a movement become so great that it affects the whole humanity with equal vehemence, and shows that, in the presence of certain elemental influences¹—even if they are not as demonstrable by our methods as are the currents of the atmosphere, enormous volcanic eruptions, inundations, or great fluctuations of temperature—all differences of race, of country, of position, of age, cease without it being necessary in such cases to assume an infection, a transmission from one individual to the other, along the route of culture and corresponding to the rapidity of traffic. Neither did cholera ever travel in the train of caravans, nor does it to-day speed with the rapidity of railroad trains, quite as little as it heeds the actual toll-gates and defensive measures which are erected to oppose its entrance over

¹ Even if influences can not be measured by our methods—*i. e.*, if they correspond to most minute currents and stimulations which as yet have no demonstrable (mass) effects upon the external media, respectively the instruments used for measuring—we are not justified in denying the existence of such influences. With the same justification we might insist upon the integrity of a photographic plate exposed to light, because the impression of light was not perceptible to us, or because no elemental events coincided with the illumination. And yet these minutest impulses of light disturb the constitution of the sensitive layer more markedly than the most violent forces of nature, a hurricane or an earthquake—influences which the strongest buildings are unable to resist.

the highroads and through the ports of entry of traffic—not unlike the person who would bolt doors and windows to protect his barometer from the fluctuations of air pressure.

Tho the inclination prevails to-day, in the era of solution of all epidemiological problems and of the victory—apparently equally well secured by strategical and tactical measures—over the majority of epidemic diseases, to pass unhesitatingly from such antiquated views (and so little confident regarding the display of our power in the realms of prophylaxis and therapy) to the order of the day, it would be well, nevertheless, for the very reason because we are so sure of our points, at least to remove all uncertain foundations for demonstration, in order not to present to the opponents of the victorious cause handles that are but too convenient for their attacks. Care should be had, above all, not to utilize the ephemeral results of insufficiently long periods for statistical decisions as to causal relations. It is, to say the least, hasty, in view of a series which so unquestionably shows the character of natural decrease of mortality, to draw a conclusion as to the special efficacy of a new, hitherto inefficacious, factor—namely, a curative serum—since there can be no question that radically different influences must concur here to shape statistics.

III

Etiological and Therapeutic Errors Resulting from Deficient Knowledge of the Law of Undulation

From the philosophic standpoint of an investigator it is deplorable, from the standpoint of the critic of human

frailty it is conceivable, that the smallness of the horizon or a peculiar idiosyncrasy of the weak children of man of boasting of the accomplishment of practical results in the rule over the laws of nature, continually becomes a cause again of ascribing the origin of certain events which take place in relatively short periods to human agencies and not to the prevalence of natural processes which accidentally (or legitimately) coincide with the tendency of our endeavors. We are, as it were, still on the standpoint of aboriginal peoples, the medicine-men of which create the belief that they are capable of chasing away, with their drums and conjurations, the moon, or an evil spirit obscuring the sun.

This tendency of ascribing to human agencies what has long been prepared by nature, and to regard processes, upon the course of which human actions exert but a small influence, as the exclusive result of human production so soon as the desired result takes place—*i.e.*, so soon as the trend of events is in the direction of our interference, or, more correctly, of our wishes—this tendency of overrating human influence is equally manifest in favorable and unfavorable results, in that certain individuals who stand, as it were, at the bifurcation of two roads and as the first are forced into the new—good or bad—direction, are either, according to the final result, celebrated as heroes or stigmatized as traitors. This applies to physicians who endeavor to rid state and society of evils, and also to those who attempt to accomplish the same end only in the individual; the inclination prevails to attribute the favorable course to the keen perception of the physician, the unfavorable one to his lack of knowledge. In the same manner as a remedy is considered an antipyretic because, administered

immediately before defervescence, it appears to be the sole cause of the change, in the same manner as often an aggravation of the condition is attributed to the therapy adopted instead of to the natural course of events, so runs also the trend of thought in epidemiological and social affairs. The inclination predominates to trace the origin of an epidemic to lack of precautionary measures toward the transmission of germs, to attribute the protection to the rigidity of defensive arrangements, altho experience teaches every day that this conclusion is a fallacy, since a fire does not ensue every time sparks are dropped, but only when combustible material is at hand, and since experience proves that only a small minority of individuals are in normal times in this sense predisposed to disease by infection.

Cholera germs are undoubtedly always present—at least, in India; for the traffic from India to Europe is approximately always the same, and is carried on in the same manner. The gatherings of pilgrims in Mecca are approximately of the same number, the pilgrims come from the same sections, and still great epidemics occur only *temporarily*. Patients with scarlatina, measles, and diphtheria, and germs of these diseases—if the affections are traced to such causes—are always present with us, but epidemics are comparatively rare—*i. e.*, these maladies have always shown distinct exacerbations and remissions without, however, disappearing entirely—at least, in the larger cities. Whence these differences? Are they due to the efficacy or inefficacy of our prophylaxis, to the power or impotence of our hygiene and therapy? Is it possible that the allegedly beneficial measures of disinfection and isolation are sometimes handled too carelessly, and does it require more experience, that of

disaster, to become wise? It is difficult here to bring about unanimity of opinion, altho the conditions are sometimes sufficiently transparent to allow of an impartial criticism of cause and effect. Every one interprets the facts from his individual standpoint. Men of action and of tangible causes believe that there is still not enough being done; others maintain that matters always run their course in the same old way, in spite of the strict observance of the well-known measures.

The conditions in typhoid epidemics are primarily to be considered in this respect; for they especially served always the purpose of furnishing, according to the prevailing standpoint, proofs for every theoretical opinion.

Let us consider the conventional course of events as it has frequently taken place before our eyes. Not until after a large number of affections has been determined (hence, after the etiological factors of typhoid fever have acted most energetically for some time), measures against the epidemic may be adopted; *i. e.*, only the sudden dissemination of the affections suggests the dangers of an epidemic, arouses the minds and incites to action, soon leading to favorable results. In other words, because soon after the determination of the presence of an epidemic, and after ordering the discontinuance of the use of the water employed so far, or after other measures, a standstill, or even a diminution, of the epidemic can be noted, it is actually believed that the *etiological factor* has been removed; for how else could the decrease in the number of affections be explained? It is not considered that the occurrence of a greater number of affections, which justifies the designation of an endemic or epidemic of typhoid fever being present, can not, in the most favor-

able case, be expected until four weeks after the beginning of the action of the specific micro-organism, or of the typhoid toxin (if this expression is to be chosen), or after the operation of any other unknown factors, since the incubation period lasts about two to three weeks, and a lightning-like rise—*i.e.*, simultaneous reaction—in all persons affected is very rare, because at first those individuals are attacked who are predisposed and subsequently those that are less so, and because the degree, respectively the manner, of the reaction—in short, the distinctness of the manifestations—is not equal in every instance. Because, further, it is not considered that only a comparatively small percentage of the population is usually affected in the general course of epidemics, and that, hence, in cases in which a great many persons have succumbed to the noxious influence, the noxa has frequently already ceased to be present or its power is about to become extinct—because, therefore, the fact is lost sight of that the noxa as well as its products represent stages of development, *i.e.*, an undulation with acme and decrementum—we fail to remember that also the natural factors may, long before our action commences, have begun to operate in the direction of our endeavors.

Of course, the development of events can only be gradual—*i.e.*, the undulations will be recognizable in the conduct of the affected population even after the extinction of the actual noxa (as the waves are visible on the water after the stone that caused them has sunk to the bottom); it will always take some time, about four to six weeks, until complete repose is established.

So long, therefore, as the principles of scientific investigation and demonstration are not more duly considered in determining etiology of typhoid fever—in objective in-

ductive investigation—the foundations are entirely *unreliable* for the usual conclusion that the drinking-water is almost always the cause of becoming affected by enteric fever; yes, the same methods of inference may be utilized, according to the prevailing fashion, with apparently the same certainty, for the determination of any other etiological principle—*i. e.*, the method which has become customary of late to demonstrate the etiology of typhoid fever is of about the same power of evidence as the conclusion that an incantation pronounced when the trees are in full bloom is the cause of the destruction of the blossoms occurring two weeks later according to natural laws. Whatever may be done upon a sudden accumulation of the typhoid cases during the acme of the endemic, it is sure to cause the termination of the disease in four to six—at most, in eight—weeks; for every experienced physician knows that the sudden rise in the number of certain cases of disease, which is called epidemic or endemic, always continues for at most six to eight weeks, that usually an increase takes place for only about four to six weeks, followed, after a short halting at the acme, always by decrease, unless most abnormal conditions, such as occur only once in centuries, upset all experiences.

The decrease of typhoid mortality (which the experienced were able to perceive as early as at the end of the seventies) was first, in fantastic overrating of medical art, attributed to the beneficial effect of hydropathic, later to that of pharmacologic (antipyretic) therapy. A determining factor for the decreasing morbidity of typhoid fever was considered to be the improvement of hygienic conditions, and, above all, the introduction of aqueducts, immaterial whether the water was obtained

by filtration of river water¹ or by means of conduits bringing the water from wells. But to him who considered the influence of the periods—respectively, of the undulations, of epidemics, it was obvious from the beginning that certain influences were already at work for a change of conditions for the better before the hygienic arrangements referred to could attain any effect.

For Breslau, for instance, Jacobi² determined regarding typhoid fever that the mortality (it is true, with certain fluctuations) has perceptibly decreased since 1868, and even quite essentially so after 1873, and he arrived at the conclusion that, for the time being, neither the influence of an improved therapy nor that of the numerous progresses regarding hygiene of water, dwellings, and soil, can be shown to have been responsible for the figures—so perplexing at the first glance—which state the betterment of mortality and morbidity. This conclusion may be endorsed according to other experiences, because the same decrease of morbidity and mortality is manifest everywhere, in small towns and in the country, in which an actual improvement of therapeutic and hygienic conditions is quite out of question. A connection between the extinction or the outbreak of epidemics and our hitherto employed methods is proved as little, in my opinion, as the connection that the victory of the German army should be

¹ In contradistinction to former views, river water (it is pretended that this water can not be sufficiently filtered) which for more than a decade was claimed to have furnished hygienic advantages, in this era of the comma bacillus is again considered the root of all evil, and it is proclaimed that nothing but the utilization of ground-water will answer hygienic principles. Why not first adduce positive evidence that cholera travels along water routes, or that infection takes place principally by water? The fact that sailors become more frequently affected—provided it is true—than others may be due to quite a number of other possibilities, the exclusion of which is not as easy as is assumed by the advocates of the drink'ng-water theory.

² J. Jacobi, Beiträge zur medicinischen Klimatologie und Statistik, umfassend die wichtigsten Elemente einer hygienischen Local-Statistik der Stadt Breslau (*Habilitationsschrift*), Breslau, 1879 [Contributions to medical Climatology and Statistics, comprising the most important elements of hygienic local statistics of the city of Breslau].

ascribed to the specific drill and not to a number of very important other factors; for here an exceedingly important part is played by imponderables—influences which for the time being are still beyond the power of our knowledge.

Hence, I believe that particularly the critical statistics of diphtheria mortality are of a general instructive significance, since they show that the action, which very nearly conforms to a certain law of external influences unknown to us, is already effective in that direction which is aimed at by friends of humanity and by physicians through hygienic and therapeutic measures. A constant undulation obtains also in the realm of disease, because the change of external and internal conditions of life, the diversity of the different generations, and even the significance of quite local effects, are greater than he is fain to acknowledge whose narrow mind believes itself to have penetrated into all mysteries of nature. Only deficient recognition of the limitation of our inferences and the inclination to yield, in defiance of experience, to the imposing impression of bold assertions, are to blame that, in cases in which it is still a question of ascertaining the cause of the events, we precipitately consider our interferences determining, instead of carefully investigating the natural course of events, or of letting the facts of experience (after the lapse of sufficient time) speak for themselves.

Nothing is more readily conceivable, but nothing more erroneous, than the desire that something must be done under all circumstances. This proposition is valid only in case we are actually masters of the conditions when we possess a true insight into their relations. Not he who claims to be able to accomplish this, but he only who is able to prove his contention scientifically is

entitled to interfere. However, proofs of the efficacy of our interferences can not be adduced, as is usually done, in that the most *obvious*, timely, or local processes are considered determining for the course of events, simply because they happen to occur within the narrow visual angle of the observer—*i.e.*, in the direction of the aim of his endeavors. Such a proceeding resembles too much that of the gnat which, when it appeared that the efforts of the horses were unavailing to drag the heavily laden hay-wagon, flew away to ease the load, and triumphed over its influence when the wagon was at last set in motion.

Statistics unquestionably furnish reliable foundations to determine certain analogies in the phenomena, which, however, we frequently designate, erroneously, as the expression of legitimate conditions, since the period for judging is mostly too short and the material suitable for truly scientific purposes is not easily procured. To obtain this solid foundation, fit for conclusive arguments, the true measure of phenomena, it is not sufficient, as is erroneously believed, to execute merely the simple arithmetical calculation correctly—to operate with the figures representing the results of the different series of observation as with indefinite quantities. Any one is in the quagmire of error who believes that he faces the clear and comprehensive structure of a simple arithmetical problem when encountering an impartial grouping according to correct principles, and adequate amounts of figures, sufficient now to allow the simple technical manipulations to be done by any one. Important as it is to group the figures correctly, and to set up the various view-points to criticize them (to consider, as it were, the tactical and strategical requirements), still all efforts are

in vain if the material is not reliable, if every factor of the calculation—each individual tactical unit, as it were—is not of an established value, and if the units constituting the larger figure are not well-defined quantities. To obtain these reliable units is one of the most essential difficulties of the statistical strategist. The strategical deployment (the strategical grouping according to the different view-points) is rapidly accomplished, especially on paper; but the building up of the individual factors, the formation and the examination of the material, requires considerable time and labor; yes, the obtaining of the material appears to be impossible so long as the handlers of the raw material, the collectors of the units, are not aware of the importance of their office and of the importance of objective criticism for the determination of simple values.

Unfortunately, therefore, many statisticians resemble high-gifted generals who lead a wretched army to battle: it is not their fault if their great combinations miscarry; the blame rests with the material which does not offer any security because the units—the individual members of the army of figures as well as the ones of real armies—and the larger figures (the higher units) do not represent solid values.

The elaboration of a scientific proof from statistical material requires time and patience, as does that of every structure, whereas the merely ephemeral decorative ornaments are rapidly finished. The unsteady structures of optimistic statisticians are rapidly destroyed; they deceive the superficial observer, but the lack of stability of their foundations is betrayed by the rapidity of their construction. Any one who means to demonstrate the significance of a therapeutic method—hence, the influence

of our interference with the course of diseases—at the hand of material collected within a brief period of time, must not be in doubt regarding the duration of his construction, however glaring and effective the rapidly created work may appear. The very form and rapidity of his demonstrations are certainly sufficient to arouse the suspicion that he is less intent upon scientific conclusions, which are sanctioned in matters epidemiological solely by the factor “time” than upon imposing assertions. The dictum, “*Nonum prematur in annum,*” holds good for the statistical confirmation of the rules of etiology and therapy more than for other matters.

The contention is fully justified that a new method in therapy will appear the more efficacious the farther the events announcing a reversion of the prevailing tendency of a disease have cast their shadows before. Skeptics or adherents of preestablished harmony might formulate this dictum for medical view-points, to the effect that a remedy as compared with former ones will act the more drastically the more its employment occurs in a period of an essential decrease of the factors constituting the dangers of a disease. This advantage was in a great measure accorded to the healing serum, and even under these conditions its efficacy remains not only far behind its original promises, which we at once characterized as Utopian, but even behind favorable results that were already accomplished at the beginning of its employment.

XXIII

OPPORTUNISM IN MEDICAL STATISTICS

I DESIRE to make some remarks in connection with the statistics of a prominent hospital which were recently published: not to utilize the figures in the same manner against the serum as in the report they are quoted in favor of the same, but to show what conclusions will be arrived at if light and shade are equally distributed—hence, if the method of deduction practised here only in favor of the serum is utilized also for the benefit of expectant or any other treatment. I feel called upon to make these remarks all the more because I regard the report of a hospital conducted on such a model plan not as a negligible quantity, but as an especially important foundation of medical statistics, in this case quite in accord with the political papers, which have not failed to avail themselves of the report, respectively of the inference, as a means of propaganda for the serum. The statistics read as follows :

Four hundred and forty-one patients with diphtheria were treated during the year under consideration; of these, 81 died = 18.3 per cent.

Of these were treated with serum, 408.

Without serum, 33; four of these were moribund.

Of those treated with serum, 75 died = 18.3 per cent.; of those treated without serum, 6 died = 20.5 per cent.

Four children were admitted in a dying condition, one child was admitted suffering from bronchopneumonia after diphtheria, and died.

Of the cases treated with serum there were :

85 severe cases, of which died 39 = 45.9 per cent.;

191 moderately severe cases, of which died 33 = 17.3 per cent.;

132 mild cases, of which died 2 = 1.5 per cent.

Tracheotomy had to be performed in 124 cases; of these died 43 = 34.6 per cent.

The treatment with Behring's serum furnished results also in the year of the report which considerably surpass those of former times, previous to the introduction of the serum. Deleterious consequences of a serious nature have never been observed.

If we accept the standpoint of the report that two groups of figures of considerable difference (408 treated, 33 not treated)—especially without statement of the reasons why a considerable number of the patients were treated without serum—are comparable—*i. e.*, can be utilized, opposing the percentile results (18.3 : 20.5)—for statistics of the curative value of the serum, it follows even from the simple comparison that no better result was obtained in those treated with the serum than in those that were not treated; for a mortality that is less by 2.2 per cent. than the other, still comes within the range of natural variations (of the limits of errors). However, a close inspection reveals the singular result that those subjected to the serum have even furnished an essentially more unfavorable death-rate. For one thing, the statistics contain an error of calculation; for the mortality of those that were not treated (33 cases and 6 deaths) does not figure 20.5 per cent., but 18.2 per cent.; it is, therefore, approximately the same as

¹ It is stated, on page 18 of the report, for one of the wards, that adults were not treated with injections, and logically, in a manner that calls for acknowledgment, all conclusions as to the curative action of the serum were declined, owing to the peculiarity of the material.

that of the patients treated with serum (18.3 per cent.). But, secondly, the addition of the moribund to those that were not treated must be called in question, since this does distribute light and shade too much in favor of the serum. Patients admitted in a moribund condition must, in our opinion, not at all be considered in therapeutic statistics of a hospital; for, when a physician pronounces a patient moribund—which, of course, he will do only after an objective appreciation of all symptoms, and because he considers recovery to be *absolutely impossible*—nothing remains for him but to employ means calculated to maintain the flickering flame as long as possible—*i. e.*, he will not make any actually therapeutic or energetic—respectively, alterative—attempts, but will only adopt analeptic measures. But whatever may be the opinion held regarding diagnosis and medical activity—even if the decision is arrived at in such cases of introducing a treatment calculated to remove the functional disturbances representing the disease, and not only to attempt the preservation of the condition of strength—this much is certain: that such patients should not be utilized as material for the compilation of therapeutic statistics, except of those of life-saving operations. For the statement that the patient is moribund is equivalent to the declaration that, to the best of one's knowledge, the organism is no longer capable, under the given conditions, of maintaining life by its functions, much less to take up the *struggle against abnormal influences* which are manifest in the symptoms of actual disease. However, highest degrees of exhaustion do not properly constitute disease, but, on the other hand, disease may sooner or later lead to such extreme exhaustion, a condition which, from the standpoint of treatment, has no

longer anything in common with the actual disease that was treated originally (sudden deaths during convalescence after acute affections, secondary maladies, etc.).

As a hospital physician, therefore (if for no other reason but to avoid furtherance of the erroneous belief still prevailing in the minds of some ignorant persons that most of the patients admitted to hospitals are claimed to succumb to the treatment), one should not utilize those for the statistics of a method of treatment who die within twenty-four to twenty-eight hours, without a therapeutic interference in the above-defined sense having appeared feasible with some chance of a favorable result. To be excluded, therefore, are those patients in whom the primary disturbances are so subordinate to the manifestations of weakness that even an operation, far remote from creating more favorable conditions for the maintenance of life, directly threatens it. The same applies to patients who, in a late stage of an internal disease, well defined at the onset, appear to be moribund upon admission, owing to most threatening conditions of weakness; these patients can no longer be objects of energetic specific treatment. Such cases should be excluded from hospital statistics, in order to create uniform conditions for the criticism of social factors and to furnish to the ignorant or malevolent the proof which, unfortunately, is still necessary, that not the hospital is the cause of deaths, but that an unusual number of patients are brought for admission shortly before death, and in a *condition that is past recovery*. This would not constitute a falsification of statistics, but means only the correct distribution of figures, which is very important when it is a question of ascertaining the influence of the various (among others, social) factors upon cure, etc.

It is true, those patients would also frequently have to be considered moribund who have become anemic as a result of severe hemorrhages, and who are so often claimed to have been kept alive by transfusion; further, those who suffer from shock in consequence of internal incarcerations—*i.e.*, the brilliant results accomplished would then not be sufficiently expressed in the statistics of those who were saved by our art. On the other hand, those asphyxiated by acute edema of the glottis or by foreign bodies would give too high a percentage for the category of the moribund—in short, the category of cured diseases would run short. However, all these objections could be met, in my opinion, if the heading “moribund” would be displaced by the classification “threatening bodily weakness or adynamia,” and naturally the subdivision into “cured,” “improved,” and “died” be retained for them. This is the very point in which the limits of our prognosis and diagnosis and the efficacy of therapy—respectively, the influence of external conditions of life—can be demonstrated best. Then all disadvantages resulting from comparisons of incomparable quantities would be omitted, and it would be most conspicuously shown in how far the measures adopted in the hospital are still suited to be helpful even under apparently unfavorable conditions. Of course, it would be necessary that, for every patient of this category, the exact duration of his stay in the hospital should be stated and every interference noted which, passing beyond analeptic measures (*indicatio vitalis*), corresponds to *indicatio causalis* (in consideration of the primary affection).

Since statistics are neither intended to sanction errors, nor to illustrate ostentatious performances, but merely to

bring out the truth, they should be handled with careful consideration, and moribund patients, for this very reason, belong to the category of neutral cases, which must not be utilized either for or against a specific method of treatment, altho they naturally maintain their significance for the general mortality statistics and for the criticism of certain social institutions. It would be well, for this very reason, not to hesitate, and to carry those that are admitted in a moribund condition under a special heading, and to open also a special column for those who recover, contrary to all expectations, but affording so much more gratification. The point in question in such cases is, at most, the acknowledgment of an error of diagnosis or prognosis, which may befall even to the best physician, especially to the hospital physician. The latter, who particularly receives a great number of severely affected patients for examination that, besides, may suffer from the difficulties of transportation and often also from marked mental excitement, is very apt, at the first examination, to mistake a transitory shock for real exhaustion of the vital powers; but that is not a cause for reproach. Yes, in the interest of such patients as appear especially endangered, it would probably be most desirable if the first examination were not made too minutely, that it were determined only in a general way whether collapse or weakness were not due to an apparent, acutely acting cause that could and must be immediately remedied only by an operation, by a specific, or by some other expert measures (hemorrhage from the genitalia, ruptured varices, foreign bodies, intoxications, etc.).

Objection will now be made that the opinion here defended is not scientific, and that, on the other hand, im-

proper use may be made of the diagnosis "moribund" when it is desired to place the special healing power of a new therapeutic method into the most favorable light; for, the more difficult the case, the greater the glory of the deed. I do not wish to defend myself against the first objection, for it is always raised when a method is proposed that differs from the accepted scheme. I wish merely to ask whether in necropsy reports, which, after all, are meant to represent the result of the most impressive and most reliable form of diagnosis, the diagnoses "Hypostatic pneumonia," "Cerebral edema," or "Degeneration of the heart," are not much more frequently proclaimed as the *final solution of a problem* than can be admitted by the attending physician who is not able to reconcile the obscure and ambiguous symptom-complex presented by the patient with this relatively simple finding. But a misuse of the diagnosis is scarcely to be expected, for it ceases at the moment when the moribund—or, let us say, the patients with very bad prognosis for the preservation of life—form a special category which does not prove anything for therapeutic statistics, since analeptic methods are not really therapeutic methods, and, besides, an otherwise strong person may, under different conditions, manifest signs of extreme exhaustion which, naturally, at once yield to a simple analeptic remedy.

If these deliberations are taken into account, then there can be no question that the four moribund patients of the report should be deducted from the thirty-three that were not treated—*i. e.*, the statistics of the number of diphtheria patients admitted for treatment must not contain the four moribund patients at all, since therapeutic statistics can consider only patients, but no indi-

viduals, at the point of death, especially when it is a question of deciding regarding the superiority of a new therapeutic method. Of course, in determining the general mortality of Berlin, these four cases must come into question, and—provided, as we assume, it is ascertained that they had not received any injections before being admitted at the hospital—they then furnish actually material in favor of the serum treatment, which, however, considering the magnitude of the figures that are involved here, can scarcely be expressed by percentages.

Therefore, only twenty-nine patients were not treated, and of these, two died; this makes a mortality of 6.9 per cent. Hence, there can not be any objection to the conclusion that—even if a *greater* number of patients were *not* treated, so that two fully identical groups could be utilized for comparison in regard to the efficacy of the serum, and if, which is not probable, the mortality had even doubled on account of the greater number—with even 13.8 per cent., it would still remain far below the mortality of those treated with serum.

Apart from this objection to the hospital statistics—it may be made not only against the above-mentioned statistics but against almost all similar ones—I desire here to emphasize several other doubts, which are also quite important. In hospitals with several wards for diphtheria patients, the final registration should be made in a uniform manner—*i. e.*, the patients of all wards, treated and untreated, should be added and compared; furthermore, if adults are at all treated with serum, the statistics of adults should be completely separated from those of children. The statistics before us are particularly instructive as to this very point. Since, according to my opinion, which is probably shared by others, true diph-

theria—*i. e.*, the disease characterized *clinically*, not only bacteriologically—in adults must be regarded as one of the most severe diseases with most doubtful prognosis, especially if the center of the pharynx and the uvula are attacked—in other cases the differentiation from mere angina may be extremely difficult; since, therefore, diphtheria in adults runs a very severe course, it would be reasonable to expect that the mortality of the adults—here not treated with serum—had been a relatively great one. But if we now note that in the second internal ward *all* men (respectively, twenty-three adults) have recovered *without* injection, whereas, of seven children who received injections, one died, it seems, according to my experience, as tho this argues quite as forcibly against the curative power of the serum as for the mildness of the present epidemics.

Accordingly, the conclusion repeatedly arrived at by me will have to be endorsed, that the slight mortality of the last years was not brought about by the serum, but that the number of the really serious cases of the disease has decreased—respectively, that the course of the disease in severe cases also is a more favorable one in general than formerly, so that the prognostic signs of former days are no longer of the same significance, as was also explained by me.

Such experiences were made also in other affections, not only in infectious diseases. Thirty years ago every patient suffering from diabetes was considered almost a candidate for death, simply because diabetes was discovered only in most severe cases with very conspicuous general symptoms. At present we think differently of glycuria and diabetes.

It is difficult, therefore, to suppress the question, What

would have become of the other (treated) cases if they, too, had not been subjected to the treatment with serum? Since, on the one hand, the 408 (respectively, 404) patients included a total of only 85 (21 per cent.) severe cases, as against 191 (47 per cent.) medium severe, and 132 (about 32 per cent.) mild cases—two categories which certainly can not be regarded as chief witnesses in favor of the efficacy of the serum, which should be tested on the severe cases—since, on the other hand, **45.9 per cent.** (!) of those succumbed who were treated for severe involvement, this result does not appear to us as being in any manner better than that of any other former method of treatment.

I had never, in former years, and even in the severe cases, calculated upon more than 40–50 per cent. mortality, and even in those that were tracheotomized, altho they usually were not made subject to tracheotomy until the situation had become critical, I did not reckon for an average of several years—for here it may occur that very considerable fluctuations take place in *short* periods—upon a higher percentage than 50–60 per cent. mortality. It should be borne in mind, further, that, at present, tracheotomies are undertaken very early in comparatively *slight* manifestations of laryngeal stenosis, so that the prognosis must become essentially better by this fact alone.

It is necessary, therefore, to consider also the following point: If the cases, upon the basis of a careful examination, are divided into categories according to severity, it is obvious that, *a priori*, a dissimilar result is expected also in the untreated cases—*i. e.*, if the enormous mortality of 40–50 per cent. is expected in severe affections, then, according to my estimation—I am not in possession

of exact statistics—we may calculate, in the medium severe cases, perhaps upon 15 per cent.; in the mild ones, possibly upon 1–2 per cent., since it occurs sometimes that a mild case develops into a severe one. I do not believe that an experienced physician formerly figured on a larger mortality in cases that were thus classified.

The result during a long period of time depends always directly upon the proportion of the severe (and perhaps of the medium severe) cases to the total number of affections—*i. e.*, there are (which is obvious to the expert) great and small epidemics (respectively, endemics) with favorable or unfavorable course, according to the quantity of the severe cases having been conspicuously large or small. The experienced physician is frequently even capable of making the prognosis of the epidemic, as it were, immediately upon the occurrence of the first cases; for the severity of the epidemic is often manifest at the onset, in that the very *first cases present abnormally severe phenomena*, and this character is maintained until the appearance of many mild cases announces the end of the epidemic. To be perfectly rational, we should, therefore, eliminate the mild cases from a statistic of therapeutic results, or, at least, classify severe and medium severe cases under one heading; however, such a selection would naturally give rise to essential scruples, since the separation of the severe cases from the mild ones is readily accomplished in most instances, it is true, but not that of the severe ones from those running a medium severe course, and that of the latter from the mild ones. It is best, therefore, to maintain the distinction between mild and severe cases. But, at any rate, it must be conceded that a mortality of 17.3 per cent. in medium severe cases, as accomplished in the

serum treatment, is not so low as to cause the method in question to appear in an especially favorable light.

If, now, the figures concerning us here would be based upon the above-mentioned approximative estimation—*i.e.*, if it is assumed that the mortality proportion of the mild to the medium severe and severe cases is as *c.* 1 (2) : 15–20 : 50—there would result, on the basis of the figures here given of those treated with serum—*i.e.*, of *ca.* 32 per cent. mild, *ca.* 47 per cent. medium severe, and *ca.* 21 per cent. severe cases in those that are not treated (respectively, treated after former methods), a mortality of C. 0 + C. 7 + C. 10 cases—*i.e.*, the mortality under equal conditions would be 17 per cent.—*i.e.*, really even slightly less than was the outcome of the treatment with serum. This result, therefore, under the existing conditions (the ratio of cases regarding the severity of the disease), must be regarded as an absolutely normal one—*i.e.*, as the result of an epidemic distinguished by a very small number (scarcely 21 per cent.) of severe cases, whereas the result is here proclaimed to be solely the consequence of the serum. Therefore, the significance attached to the number of the severe cases is manifest also here; for, if only 19 per cent. more of severe cases had been present—*i.e.*, for instance, 40 per cent. severe, 27 per cent. medium severe, and 33 per cent. mild cases—respectively, 40 per cent., 47 per cent., 13 per cent.—had been treated, the mortality would have been *ca.* 20 + 5 + 0 cases (per 100) = 25 per cent.—respectively, 20 + 8 + 0 = 28 per cent. It increases, therefore, materially by relatively few severe—respectively, medium severe—cases—*i.e.*, by about 47–65 per cent.; whereas, upon decrease of the severe cases—hence, with about 10 per

cent. of severe, 47 per cent. of medium severe, and 43 per cent. of mild cases—it only amounts to *ca.* $5 + 8 + 0$ cases = about 13 per cent.

If from these figures the conclusion is arrived at that the treatment with the serum of Behring has furnished results also in the year of the report which considerably surpass those of former periods, previous to the introduction of this remedy, than even an opponent of orotherapy may acquiesce to this dictum, altho with a few side remarks. It would be necessary for him to insist upon the supplement—not pleasing, it is true, to the serum enthusiast—that also the non-treatment, respectively expectant treatment, but in any case the treatment WITHOUT SERUM, at present also furnish results which not only considerably surpass those formerly achieved with expectant treatment, but which are even far superior to those obtained from the treatment with serum.

This dictum, however, proves the justification of the view which I put forth immediately upon the publication of the first report concerning the brilliant results of the serum—namely, that the decreased mortality was influenced not by the serum, but by a number of other factors which are not sufficiently appreciated by medical opportunity statisticians and which ameliorate the dangerous nature of the disease, respectively of the severe cases. I could even *a priori* exercise this criticism, since, in my opinion, neither the theoretical foundations of the orotherapy (the theory of protective inoculation has nothing in common with the theory of the curative effect in disease), nor the method of its application practised so far, can stand in the face of scientific criticism and of clinical experience. The view which logically and in accordance with experience was alone justified,

that the reason for a sudden rise or fall of mortality must not be looked for in our medical interference, but, above all, in external factors, respectively conditions of life, which are still to be explored, but are not explored as yet—this view alone can protect from overvaluing or underrating of therapeutic (respectively, hygienic) methods. But this view is always forgotten, in an unscientific, tho explainable, manner, when it is a question of proving the quality of our performances by the degree of decrease of the diseases; whereas, quite in contrast to this neglect, it is most warmly defended when intending to explain the increase of mortality. Then the influence of overwhelming, unfortunately as yet unknown, factors or powers of nature is acknowledged, in opposition to which medical and hygienic performances become inferior in value, which can not be lauded too highly in favorable times when assumedly nothing is concealed from us, when we *appear* to have struck at the root of the evil.

Thus the same report states, in contrast to the inferences regarding the value of the serum, but, in our opinion, deservedly so: "The mortality in typhoid fever amounted to 21 per cent. as against 16.7 per cent. the year before, which, in view of the fact that the principles of treatment have remained the same, must be ascribed exclusively to the greater severity of the cases admitted." This conclusion, according to the present state of our knowledge, is the only justifiable one, and, because it is, we should not under favorable conditions rest upon imaginary laurels and attribute to our performances the glory which we owe to the weakening of unknown factors. We should, rather, in accordance with the principle, "*Si vis pacem, para bellum,*" strive for the recognition of the causes and influences to which our

performances do *not by any means answer as yet*. It is easy to boast of our strength when no assailant is present or when the aggressor is weak.

If, therefore, we, as physicians, claim the right to regard the particular intensity of the pathological process as the true and unavoidable cause of the increase of mortality—respectively, of the inefficacy of the therapeutic efforts against the power of typhoid fever—this right should not be denied to those who are inclined to attribute a pretendedly extraordinary improvement of the conditions of recovery not to an imperfect and unproven method, but to a diminution of the power of those factors which, if but somewhat developed, disturb the function of the organism and then essentially endanger the lives of many. The right should not be denied to the opponents of the serum, or, rather, to the skeptics who insist upon actual proofs of the curative power of the universal remedy, to deduce the improvement of mortality from the decrease of certain factors which weaken the resistance of the individual or produce a certain functional disturbance, so long as all other possibilities of explanation are not excluded. But this proof can be adduced only by time and by strictest criticism, since, in our opinion, in statistics as well as in war, not the great number in itself, but the intrinsic value of the individualities composing the troops and the mind that groups them are decisive. That so often only the number in itself and not the value of the unit—the statistical soldier, as it were—is sufficiently considered, is what renders statistical contentions so unreliable, and medical statistics in particular a playground of opinions.

I do not know whether these explanations will occasion the therapeutic enthusiasts to ponder over the difficulty

of medico-statistical investigation, the importance of which I rate very highly when critical methods are employed which scrutinize the value of the unit. I am sorry to say that I do not believe it, and I would be very well satisfied if he who beholds nothing behind the veil of Sais, or who can not believe what he desried to be the truth, is credited at least with an honest conviction, and not be reproached with grudge, malevolence, blindness, or ignorance. He especially who, like the author, had the opportunity of practising much therapy—altho not always in the modern sense under the device, "*Fiat medicatio, pereat ægrotus*"—is happy, even if he may be the greatest skeptic in all matters, in possessing a true remedy. Only he will not accept it with a blind enthusiasm and with denial of the criterion of his experience and of biological laws, but he will investigate whether or not surrogates or sentiments have been recommended instead of infallible, scientifically established methods.

XXIV

THE CONTENTION ABOUT FIGURES IN MEDICAL SCIENCE

I CONSIDER it necessary to enter briefly into the reply of Dr. Körte, because he entirely mistakes the principal objections which induced my criticism. I do not understand how it can be disputed that in the report criticized by me a conclusion is drawn regarding the efficacy of ootherapy by opposing two different series of treatment; for the figures placed alongside of each other are utilized for comparison, whether so intended by the author or not. Since, besides, it is distinctly stated that "the healing serum has furnished results which considerably surpass the results of former periods previous to the introduction of this remedy," I was fully justified, in my opinion, in saying that shade and light were unevenly distributed; for the new method shines so brightly only upon the dark background of former bad results. Neither is a comparison with former periods permissible, according to my opinion, as long as a possibility exists that the epidemic has in the main become milder. This is the point at which my criticism begins. And that not only the possibility but the certainty obtains that this is the case is proven, besides by other explanations of my criticism, by the fact contained in the statistics that the untreated cases also had furnished a similarly favorable result—a result which also surpasses that of

former years by a great deal. If, now, the same favorable results are accomplished without, as with, treatment, it follows that the epidemic has become milder, and the proof adduced for the importance of the method of treatment entirely illusory.

Whether we are here dealing with small or large numbers is of no consequence, for there is no longer any possibility, according to my opinion, with the exclusive treatment with serum at present to utilize the more favorable character of the epidemic for other methods or for nature's healing. The chances benefit merely the serum treatment, and the true character of the epidemic can be studied only when a favorable accident is the cause that a number of patients are not treated. In this connection, however, the number of thirty-three patients is not at all small.

What I request is precisely that we once more attempt to obtain large series of observations without curative serum; but we should make haste in doing so, since a change in the character of the disease may again take place. Even now, if reliance can be placed upon the reports of the daily papers, small local epidemics become apparent which show an unfavorable character, in that the number of the fatal cases becomes larger. The exacerbations of mortality during the periods of the year 1894, when the amount of serum on hand ran short, as opposed to the periods of treatment with serum, are not conclusive evidence, since at that time a certain selection was made among the patients to be injected, and the severe cases and those that were moribund were counted among the untreated, whereas scarlatinal diphtheria was deducted, etc. According to former experiences—and there are at present signs in that direction—it may be

predicted, should the severity of the individual diphtheria affections again increase, that the cases with unfavorable termination, as mixed infections, will no longer be taken into account in the statistics to determine the question as to the value of the serum, whereas those cases that run a favorable course, even if they are mixed infections, will, nevertheless, then be utilized as proof in favor of the action of the serum. And thus it will occur—since, as previously emphasized by me, a specific bacillus does not exist or possess a protean nature—that finally only those cases will be considered to be diphtheria which are cured by serum; for this cure must be the best and only proof in the eyes of the dogmatists that the specific bacillus was actually present. Since otherwise the entire theory would collapse, endeavors are made even now to show that the serum acts principally as a stimulant which supports the vital energy or tissues in the struggle against disease, and it is employed also in cases that have no longer anything in common with diphtheria.

In the present state of affairs everything in favor of the serum is continually emphasized, whereas whatever argues in favor of the other methods is either buried in silence or not considered at all. If any quack would today maintain that his method accomplishes essentially better results in the treatment of typhoid fever than that of former years, the fact would indignantly be pointed out that all other methods, or, rather, the scientifically approved methods, had likewise furnished considerably better results during the last years, when the course of typhoid fever had become so much more favorable. It will certainly not be forgotten, when arguing with others than physicians, to designate a conclusion in which light

and shade are not equally distributed as sophistic or as not objective.

It is entirely immaterial, under present conditions, whether statistics are published for scientific purposes or merely as a statement of accounts, as it were; for figures are always utilized by one side or by the other according to their apparent results, as is plainly shown by facts. In fact, a favorable opinion has even been based upon them in the statistics in question—*i. e.*, in the statement of accounts not directly serving scientific purposes; hence, scientific and practical conclusions have been drawn which, owing to the place from which they emanate, may claim special authority. Bare statistics, or such as are assumedly compiled after scientific principles, have their advantages and disadvantages; but I prefer the bare ones to those which, for the greater glory of a certain method are trimmed (respectively, draped), in that, for instance, the unfavorable cases are eliminated by a trick, etc. I remind merely (other examples need scarcely be quoted) of the statistics concerning death after operations (respectively, in chloroform narcosis), which, in our opinion, is exceedingly often unjustifiably attributed to feebleness of the heart and inflammation of the lungs; further, of the first statistics regarding the effects of the serum, according to which the mortality had fallen to below 5 per cent., owing to exclusion of unfavorable cases or to the selection of brief periods; finally, of the statistics of the results of the cold-water and salicylate treatment of typhoid fever.

For the very reason, therefore, because all statistics with their bare figures are intended to furnish a certain basis for conclusions (I do not understand for what other purpose they should be published), such publications

should be made with care. If my criticisms were to accomplish nothing but that mere statements of accounts will furnish only the figures without comment, whereas every heading of a disease accounts separately for the patients that were moribund and not being treated, and that, in cases in which it is essential, the patients who died and those that recovered are registered according to the individual days of admittance, much would be accomplished. If this were complied with, expressions as contained in the report and absolutely incomprehensible would then be impossible. For, when it is said, "Treated without serum were 33; of these were moribund, 4; of those treated without serum, six died," then every one must believe that the moribund patients were included here, and that, after deducting them, the mortality was two.

No animosity whatever is attached to my critical remarks, but I have too great a regard for numbers to look upon my statistics as a negligible quantity. Moreover, I have often enough pointed out that as physician and as man I rejoice in the discovery of an effective remedy, but that as scientific physician and investigator I must oppose every and all statistics that mean to prove something not in accord with biological, fundamental postulates. Of such a character are therapeutic theories built upon an insufficient judgment of the reactive conditions, and promising a panacea and miraculous remedy. Just as if the complicated pathological process in its various stages, and even in the stage of inception, were nothing but a condition of increased acid or alkaline reaction, or a condition of a conspicuously marked expression of some chemical affinity, a chemical hunger, as it were, to be allayed by a sufficient complex of opposite affinities

in such a manner as to render the neutralized (saturated) organism—to use this short expression—at once identical with a convalescent person. I regard medical activity as a difficult art, and, therefore, I take every one who promises us a specific remedy against a disease, or a pathognomonic symptom, to be quite as Utopian as the one who looks for the philosopher's stone against all diseases, or who bases diagnosis and prognosis upon the microscopical examination of the excretions, as is done by modern bacteriologists (diagnosis *in absentia*).

I consider the belief in such symptoms and in specific signs and cure-alls to be, further, one of the most important reasons for the social decline of the medical profession, as I have repeatedly explained; for, if a disease may be diagnosticated *in absentia*, as it were, from a particle of excretion, and if there are specifics against every microbe, we no longer need physicians, but only technicians and mechanics who execute what every layman believes to recognize and to be entitled to demand of the physician. One of the most essential temptations to homeopathic treatment is probably contained in the possibility of finding a remedy for every symptom by consulting a book.

Theoretically it is not impossible to find for many cases a remedy or a serum which, for a short time—taking chances on other dangers—protects from affection; however, it can not be reconciled with our knowledge—which, after all, is quite respectable—of the processes in the human body that a possibility exists to find a remedy which cures every diseased individual, even if he comes under treatment ever so early. What we call the first symptoms of disease, which, as is well known, arise only after a stage of latency lasting for some time,

and of an entirely heterogeneous character and of different intensity, is nothing but a form of reaction already different in the various instances, which to remove *one* remedy is usually insufficient, since this presupposes only *one* possible form of reaction, quite apart from the fact that irritation and visible reaction, generator of disease (irritation), and symptom are frequently no longer in an appreciable relation. Such a remedy must even act deleteriously if it is applied in cases in which another than the assumed form is already present—*e.g.*, a secondary or indirect reaction. However, we can not here pursue these important deliberations any further, since we have given them more exhaustively on another occasion.

The assumedly most acute weapon of the tachy-therapeutists—*i.e.*, of the modern medical mechanics, or “chemiaters,” whose therapeutic theories result from mistaking of the scientific foundation of the disease—is acute statistics; for they are called upon to impress by striking results and to influence public opinion, instead of being convincing. This is the reason why to-day, when physicians are thoroughly opposed to critical considerations which would, from the very beginning, coolly dispose of Utopian hopes, it is imperative to devote our full energy to the purpose of showing how insignificant the otherwise edged weapon of statistics is in the hands of optimistic, or, what is quite as bad, of indolent, statisticians. The struggle for true statistical results is the struggle for knowledge, for truth itself, and only he will call such a struggle paltry or useless who is not capable of appreciating the relations between occurrences and figures, the criterion of all things, the foundation of the law of nature.

XXV

UNDULATIONS OF EPIDEMICS, AND THE SERUM OF DIPHThERIA

I

**An Effect of the Serum upon the Specific Diphtheritic Process,
Especially upon Laryngeal Stenosis, is not Demonstrable**

DR. CUNO published, in No. 20 of the *Münchener medicinische Wochenschrift* of 1901, the results of diphtheria treatment in Dr. Christ's Children's Hospital, conducted by Dr. Glöckler, during the years 1893-1900, to prove the striking curative action of diphtheria serum (see the following table). The proof appears to be extremely striking indeed at the first glance; for, whereas previously the mortality amounted generally to much over 30 per cent.—yes, even up to 40 per cent.—and during the first three quarters of 1894, when no serum was employed, to an average of 36 per cent., it declined during the fourth quarter, with exclusive use of the serum, to 8 per cent., and it reached 11 per cent. only once during the following years. Quite as extraordinary appears also the fact that, for instance, even in 1893 it was necessary to perform tracheotomy in 25 per cent. of the admitted patients, owing to stenosis of the larynx, with a mortality of 64 per cent., whereas in the first quarter of serum treatment only about 10 per cent.—it is true, with a

mortality of still 44 per cent.—and in the following year only 8 per cent., with a mortality of 17 per cent., were operated. Thus the author may apparently justly claim that “the figures must convince even the greatest skeptic of the efficacy of the serum, and that the favorable results can in this case scarcely be attributed to the less malign character of the disease.” And yet an exact analysis of the figures, which I have undertaken in connection with my former works criticizing serum, yields a result which thoroughly shakes this conclusion—yes, causes it to become void—and permits the dictum to appear justified that the curative action of the serum would seem to be very problematic, or really illusory, even to the optimist, if it had been first employed in the first quarter of 1895 instead of the last quarter of 1894.

Curve I (the undulation of the mortality figure) already evinces a very noticeable tendency to decline, a distinct decrescendo of the apices since 1888—hence, a decrease of the severity of the epidemic. If this were the curve of a typhoid-fever patient, we would be fully justified in looking for an early cessation of the fever, and, as an objective observer, would greatly hesitate to attribute the cause of this sudden, more marked decline to an antipyretic administered during this period of visible defervescence. But since the decline is considerable and actually surprisingly great only with the beginning of the serum treatment, during the fourth quarter, this curve naturally is not yet sufficient to allow of a conspicuous proof against the effect of the serum.

But if we now consider Curve II with the percentage of the patients in whom tracheotomy became necessary,

IN THE YEAR	I	II	III	IV	V	VI	VII	VIII	IX	
	Received	Died	Mortality in per cent. of patients received ¹		Percentage operated of those received ¹		Mortality percentage of the operated ¹	Mortality of tracheotomized in per cent. of admitted ¹	Per cent. relation of deaths from and after operation for laryngeal stenosis to general mortality ¹	
			I-II	I-IV	I-VI	I-VI				II-VI
	Operated for stenosis		Percentage operated of those received ¹		Mortality percentage of the operated ¹		Mortality of tracheotomized in per cent. of admitted ¹		Per cent. relation of deaths from and after operation for laryngeal stenosis to general mortality ¹	
1884	58	24	45	23	44	18	78	34	75	
1885	55	20	36	22	40	16	72	29	80	
1886	88	25	29	27	30	22	87	25	84	
1887	105	35	33	26	25	20	77	19	57	
1888	86	40	46	33	38	20	60	23	50	
1889	121	48	39	41	33	32	78	26	66	
1890	247	89	36	73	30	40	54	16	44	
1891	337	110	32	97	29	61	63	18	54	
1892	301	102	34	78	26	57	73	19	56	
1893	290	127	43	77	25	45	64	15	35	
1894 {	I. Quarter	84	30	36	27	32	14	52	16	47
	II. "	73	30	41	16	20	9	56	13	30
	III. "	57	18	31	8	14	2	25	14	11
	IV. "	87	7	8	9	10	4	44	4	57
1895	295	28	9	23	8	4	17	1	14	
1896	170	18	10	29	12	9	45	5	50	
1897	158	11	6	19	12	2	10	1	18	
1898	152	16	10	18	12	8	44	5	50	
1899	223	26	11	37	16	19	51	8	73	
1900	172	12	7	38	22	9	23	5	75	
1901	147	15	10	30	30	10	66	6	66	

¹ Fractions of percentages not stated; the figures for 1883 are omitted, owing to their smallness.

it will be strikingly shown that the necessity to perform tracheotomy has become continually less in the course of years, that the imminent chief danger of diphtheria, stenosis of the larynx, has from natural causes decreased regularly and remarkably. But this removes the principal proof of the action of the serum—namely, that the early use of the remedy prevents the occurrence of stenosis, and also favors the success of the operation; for it is impossible to show more clearly than by the character of the curve that the danger of the appearance of stenosis

was not extraordinarily reduced by a remedy or even by the serum, but by the natural course of events, so that the figure of the third quarter of 1894 differs but slightly from that of the first serum quarter. And, likewise, the chances of the operation have not been improved by the serum; for Curve III shows distinctly enough that also the mortality percentage of those operated upon was long before under the same favorable influence, and that the mortality of the operated was the lowest observed up to the present as early as during the third quarter. This proof becomes still more conspicuous by the results of the following years which, in spite of the serum, again show an ascending wave—*i.e.*, an aggravation of these conditions, and, with it, an influence of deleterious natural factors. The share of tracheotomy cases in the total mortality (see Curve IV) has again risen in the very era of the serum, and attained the height of the most unfavorable years; and even if a few cases in small figures cause a great percentile difference (see below), this fact must give us cause to reflect, and leads to the supposition that, unfortunately, an essential factor of the danger of diphtheria, stenosis of the larynx, gradually increases again.

There can be no doubt, therefore, that, so far as stenosis of the larynx is concerned, not the serum, but the natural undulation of things—*i.e.*, the so-called genius epidemicus—has been essentially active in the favorable formation of the curve, and without hesitation we may postulate, little gratifying as it may be to the defenders of the curative action of the serum: Not for the patient, but for the reputation of the method, was it a matter of great luck that the injections were begun in the fourth quarter of 1894, and not postponed until the year 1895.

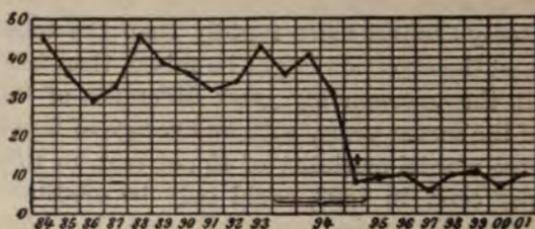
II

Significance of the Croupous (Exudative) and of the Septic Factors for the Character of Diphtheria Epidemics

But Curves V¹ and V² show that the mortality of tracheotomy declines more rapidly than the total mortality, and the objection might be raised, therefore, that, after all, the uncommonly great difference of the mortality of the serum years, with an average of 9 per cent. as against a total mortality of 45 per cent. in 1884, and of 43 per cent. in 1893, could only be credited to the serum, since the natural course of events has influenced merely an unessential factor of mortality, the localization in the larynx. But this objection is not a thorough one; for a glance at Curve IV—which shows the proportion of deaths after tracheotomy to the total mortality—teaches that, at least between 1884 and 1892, the deaths from diphtheria of the larynx (respectively, subsequently to the operation) bore the lion's share of mortality, and that this is again the case in the era of the serum. If, therefore, during the years 1884–1887 the conditions regarding stenosis mortality had been as favorable as in subsequent years, and especially in the second and third quarters of 1894; if, therefore, it were permissible to deduct the number of patients who died after tracheotomy (which possibly do not even include the total number of individuals who succumbed to stenosis of the larynx), with more than 75 per cent. of the total mortality, then the total mortality at that time would already have been less than 10 per cent., and in some years it would have reached not even 6 per cent.

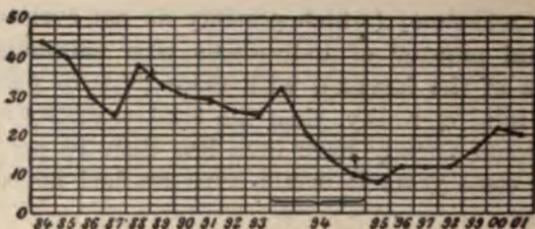
I*

Mortality of patients admitted in percentages.
(Column III of the table.)



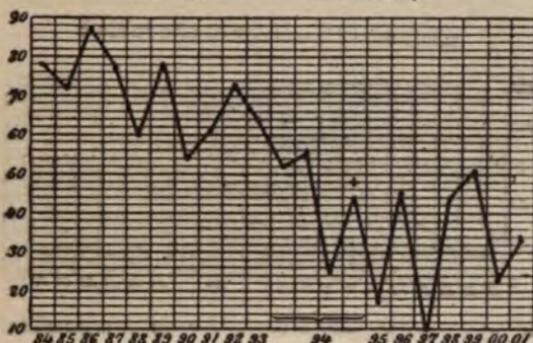
* All curves show the fourth quarter of 1894, when serum was first and exclusively used, marked by +; ~ designates that the year 1894 is divided into four quarters.

Percentage of those that were admitted and tracheotomized.
(Column V of the table.)



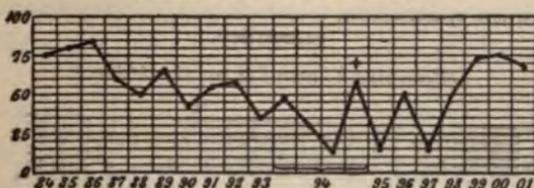
III

Mortality percentage of those that were operated.
(Column VI of the table).



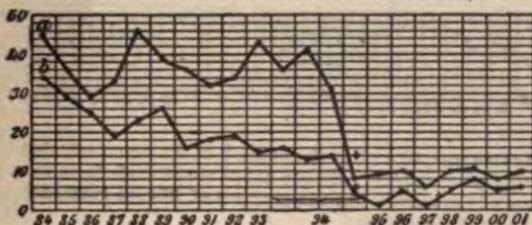
IV

Mortality of the tracheotomized as percentage of the total mortality.
(Column IX of the table.)



V¹

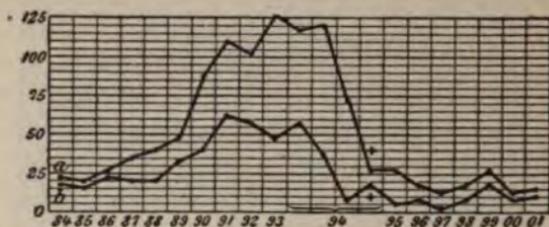
a Mortality percentage of the admitted.
b Mortality after tracheotomy in percentages of the admitted.
(Columns III and VIII of the table.)



V²*

a Mortality of the admitted
 b Mortality of the tracheotomized } in absolute figures.

(Columns II and VI of the table.)

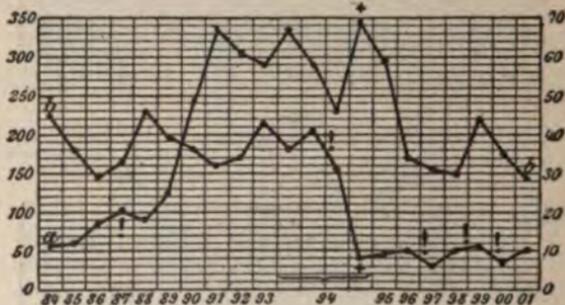


* The figures of the individual quarters of 1894 are multiplied by 4.

VI†

Law of the contrasting course of morbidity and percentile mortality.

(Columns I. and III. of the table.)



† The curve marked a gives the number of the admitted; that marked b, the mortality percentage. A division line of the ordinals for $\alpha = 10$, for $b = 2$. The figures of the curve a for the quarters of 1894 are multiplied by four, to obtain comparable ordinals.

However, such an assumption is, of course, admissible only for the respective years, as evident from the Curves III and IV, with a stenosis mortality of 75 per cent. to 84 per cent. of the total mortality, but not for the other years, and least of all for the nineties. As important as is the share of stenosis of the larynx in mortality, still, as mentioned above, Curves V' and V' show that, beginning with 1888, the curve of the total mortality as against stenosis mortality evinces a relative rise—respectively, that to the decrease of deaths from stenosis corresponds a remarkably small diminution of the total mortality. Whereas, therefore, the danger of laryngeal diphtheria becomes regularly and essentially less and even conspicuously small, the total mortality remains quite high, altho the latter also, as shown by Curve I, manifests a distinct tendency to grow less. But since the enormous decline just for the fourth quarter of 1894 can not with certainty, or even with some degree of probability, be inferred from this tendency, the adherents of orotherapy may, with some appearance of justice, maintain that the remarkable diminution must be attributed to the serum. And for the very reason because a certain proof can be adduced that the successes in laryngeal stenosis—respectively, in tracheotomy—are quite wrongfully ascribed to the serum, the serum therapists will so much more strongly emphasize the miraculous effect upon the other manifestations of the diphtheritic process. And yet weighty theoretical reasons argue also against this assertion, and we shall endeavor to demonstrate them, altho we are aware that deliberations are not cogent for the matter-of-fact men or for the *post hoc, propter hoc* investigators.

Two principal dangers are connected with the diph-

theritic process—namely, stenosis of the larynx with respiratory insufficiency, and gangrene (most intense local necrosis with subsequent sepsis), for which conditions we shall leave it undecided in how far local insufficiency of the affected organs or a constitutional disorder (intoxication, decomposition of the blood, microbiohemia) is a cause of death. Aside from these two forms which, in our opinion, can almost without exception—*i.e.*, apart from a small number of mixed forms—be readily determined by an experienced physician from the nature of the membrane in the throat, the other causes of death (acute paralysis of the heart, deglutition pneumonia, acute nephritis) are of very slight importance—*i.e.*, the character of the epidemic or its mortality never depend upon them. Besides, both forms of diphtheria are probably in a uniform manner accompanied with paralysis of the heart, which may quite as well be a consequence of an especially intense localization of the diphtheritic process in the myocardium—respectively, an effect of the diphtheria toxin (?)—as also a sequence of sepsis, or only the expression of exhaustion of the organism after the struggle is over.

Every experienced old physician who has witnessed great epidemics at various periods and at different localities, is probably aware that the individual epidemics differ materially, in that on one occasion the stenotic, at other times the gangrenous or septic, process is especially manifest, whereas both processes have an equal share in the mortality in other epidemics. Curves V¹ and V² evince that the epidemics at the beginning of the eighties were principally of a stenotic character, that even in the middle of the eighties sepsis and stenosis acted equally disastrously, and that sepsis impressed its

stamp upon the epidemics from the beginning of the nineties on; for, altho the danger of the stenosis became continually less, the mortality remained still high, in spite of an undeniable tendency to decline. But we can infer from the curves that, as early as the middle of 1894, the *hitherto determining factors of mortality also had diminished in intensity*; for the percentile mortality of the admitted has already decreased essentially below its highest point (from 46 to 31 per cent.). However, important above all is the result of Curve VI; for this shows that from the first to the third quarters, 1894, for the first time in many years the diminution of the mortality percentage corresponds to an essential decrease of the number of cases of the disease. This condition deserves the greatest consideration, since it announces a relative increase of the mild cases—a harbinger, as it were, of a material transformation of the character of the epidemic in the direction of benignity, as I have indicated in my former remarks, and as I desire to explain more in detail in the following.

III

Law of the Opposite Course of Morbidity and Percentile Mortality

If we analyze a sufficiently large, uniform, and similar material covering a long period of time, it is not difficult to determine that the curve of morbidity and that of percentile mortality usually move in opposite directions. If the former rises, the second declines, and *vice versa*; or both diverge if the mortality rises, and they converge if it declines. For instance, if ten patients die of

one hundred cases—hence, with a death-rate of 10 per cent.—then, for the following year, the case (of the three possibilities of the mortality rate) that the curve of the mortality percentages runs parallel is extremely rare; and likewise is the case relatively seldom that the mortality curve rises or falls in the same sense as the morbidity curve—*i.e.*, moves 'approximately parallel to the same (upward or downward), as in those places which, in Curve VI, are designated with an exclamation point (!). As a rule, convergence or divergence of both curves takes place. Suppose, therefore, a complete system of undulations of the epidemic—*i.e.*, a sufficiently great number of individual waves or years—is made a subject of investigation, it will be seen that, of the above-mentioned three possibilities of the course of the curve, the case of an opposite course is by far the most frequent occurrence—hence, may be regarded as somewhat in the nature of a norm; *i.e.*, if in the following year the morbidity of 100 (with the death-rate of 10) rises to 150, the percentage of deaths will, as a rule, remain more or less *below* 10 per cent., and if the number of cases declines to 50, the mortality will be considerably *above* 10 per cent.

Hence, the law of the opposite course (of morbidity and percentile mortality) emphasizes the fact that a dissemination of the epidemic, which naturally increases the chances of the individual of becoming affected, diminishes the danger to the life of the patient, whereas a decrease of morbidity, altho it lessens the prospects of the individual of falling sick, still enhances the chances

¹ To render the characteristic course of the curves particularly distinct, it is practical to select a different scale for the curve of the mortality percentage; we have adopted the proportion of the ordinals 5 : 1.

of a fatal termination—respectively, impairs the chances of recovery. This law is most distinctly manifest in the statistics interesting us in Curve VI; for an exception¹ is found only once in the antiserum time (compare the ! mark) from 1886–1887; *i.e.*, both curves run *crescendo*, whereas the mortality curve should run *decrecendo*. This abnormal condition appears to be, indeed, a precursor of the deleterious change of the character of the epidemic during the following years; for, in spite of the decrease of stenosis mortality, the mortality curve remains comparatively high. Necessarily, therefore, toward the end of the eighties a deleterious factor must have again become active, which completely abolishes the advantage gained by the decrease of laryngeal stenoses and their dangers. The second exception to the rule, but in an inverse sense, is noted in the third, antiserum, quarter, in which the mortality and morbidity curves once again move in the same direction, but *decrecendo* in this instance, whereas the mortality should really have moved *crescendo*, a conduct which, in our opinion, now indicates an essential improvement of conditions—in the same manner as the previously mentioned state announces an aggravation. This favorable change is, indeed, manifest in the fourth quarter (serum quarter), which probably shows the highest figure of cases of the disease as yet observed (in the course of three months), with exception of the quarters of 1891; but, unfortunately, it is of course impossible conclusively to prove the correctness of this conclusion, owing to the interfer-

¹ Attention may once more be called to the fact that it was necessary to consider the quarters as years, as it were, and, accordingly, to quadruple the figures, to render a comparison feasible of the figures of 1894 obtained under the influence of (assumedly fundamentally) different therapeutic actions during periods that will not allow of comparison.

ence of the serum-treatment occurring most opportunely to the serum therapeutists, because happening at the very time of the most marked change. For, altho it offers a great deal of probability—yes, certainty—to an unbiased observer, so long as the above-mentioned law is not confirmed throughout—respectively, acknowledged as the expression of an approximately regular proportion—the serum therapeutists, as exact politicians, are unquestionably justified in regarding, for the time being, the opportune coincidence of the remedy and of the conspicuous improvement of conditions as a support of *their* views, instead of as a confirmation of *our* hypothesis. However, this hypothesis is favored by the further course of the curve, which from now on—*i. e.*, during transition of the, in our opinion declining, system of undulation into a new one shows a remarkable inconsistency of the norms that prevailed so far, and—which is of especial importance—forcibly illustrates the inefficacy of the remedy with reference to the laryngeal process. Namely, a remarkable similarity again exists between the initial and the terminal portions of Curves V¹ and V² (1884–1889 respectively 1895–1900); the proportion of stenosis mortality to general mortality—respectively, to the number of patients admitted—again becomes the same as formerly; *i. e.*, stenosis again has an overly great share in the mortality (up to 75 per cent.); only the level of the curves, corresponding to the mortality figure, in our opinion essentially diminished by favorable circumstances, is a different, lower, one.

Summing up the course of the undulation system, including in this instance almost two decades, we find: After at first (at the beginning of the eighties) the typical croupous process, characterized by affection of the

larynx, and then, for a long period of time, septic diphtheria, had the lion's share of mortality, an essential improvement of conditions began from the middle of 1894 on—i.e., a well-defined valley wave of the total mortality which, in our opinion, was announced long before the valley wave which manifested the diminution of the danger of stenosis (or the mortality of those that were stenosed). But, unfortunately, the indications are at present that we again are in a stage of transition to a new mountain wave, again announced by the relatively great stenosis mortality—in spite of the employment of the serum. If the material upon which these statistics are based would be analyzed thoroughly and with due consideration of the primary picture of the disease and the course of the individual cases in their different phases since 1884, it would most probably demonstrate the correctness of this conception of a changeable genius epidemicus—respectively, of the periodical influence of certain factors changing the character of the epidemic. At any rate, according to my own, quite considerable, experiences, gained, it is true, in another province, I have long ago come to a definite conclusion regarding the character of the diphtheria epidemic of the last twenty years, and which is embodied also in the above statements.

IV

Pathogenic Remarks Regarding Septic Diphtheria, and the Possibility of its Being Influenced by the Serum

Assumed, but not admitted, that the rapid decline of the curve in the fourth quarter of 1894 was not caused

by the natural course of events, but by the serum, we would, in view of the great probability that the septic character of the affection determined also the mortality of the serum year and of some of the following years, arrive at a most paradoxical, and, therefore, remarkable result: The panacea created by an "ingenious theory" by means of a specific method as an infallible natural weapon—hence, to be employed as early as possible—against specific diphtheria (or, to express it more exactly in accordance with modern views, against the products of the specific bacillus); this specific remedy fails completely if brought in contact with the genuine diphtheritic process (respectively, its characteristic form and localization), and displays its chief action in gangrene or sepsis, which can by no means be designated as a product of the specific diphtheria bacillus, representing merely an abnormal result which is relatively often observed in this form in inflammatory or infectious diseases. If any one should dispute this, we say to him that, in our experience, first, diphtheria which has assumed a gangrenous or septic character can no longer be differentiated from gangrenous- (or septic-) phlegmonous angina, and, secondly, sepsis is one of the rarest terminations, especially in typical cases, of diphtheritic affections (with whitish yellow firm membrane and without involvement of the posterior pharynx or of the nose).

Hence, the efficacy of the serum extends, singularly enough, only to cases which, in the most favorable instance and if devoted to an orthodox bacteriological conception, must be designated as mixed infections—to cases, therefore, which can be classified only as scarlatinal diphtheria. This variety of the disease has as little in common with (typical) diphtheria as has angina

phlegmonosa, which frequently leads to gangrene and quite often to sepsis, whereas simple angina is not rarely the cause of the mildest form of pyemic affection, of acute articular rheumatism. To prove this assertion, the following deductions may be permitted: As a patient with pneumonia may succumb to pulmonary abscess, empyema, or sepsis; a patient suffering from measles, to the sequelæ of the general disease, or to bronchopneumonia, or to general tuberculosis; as sepsis may develop in connection with any form of wound or with an affection of the throat, so may also a septic—respectively, gangrenous—process supervene upon diphtheritic angina (the especially severe form of inflammation of the throat), and the more readily so, the less the primarily affected—*i.e.*, the abnormally irritated or paralyzed—tissue is capable of warding off other noxæ—respectively, of preserving its own existence. In other words, the less a typical (croupous, hence superficial) exudation—*i.e.*, an adequate, and, as far as the prevention of the general affection is concerned, probably favorable, reaction to the noxa of diphtheria is brought about, owing to a certain weakening predisposition depending upon the natural tendency or upon the *genius epidemicus*, the less pronounced the membranous, or, better, the extramucous, character of the products in the pharynx as against the intramucous (destructive) process, the more certainly is the occurrence of intense necrotic and septic disturbances to be expected.

What, then, constitutes the difference, for instance, between croupous (fibrinous) bronchitis, or croupous pneumonia, with critical resolution, and pulmonary abscess, or gangrene, if not the faculty of the tissues of maintaining their capacity of existence under the influence of an abnormal irritation—

i. e., under altered conditions of irritability and nutrition, or under the pressure of the exudate; hence, to organize an appropriate compensatory labor for the affected parts or the entire organism, in spite of the disturbance? On the other hand, the tissues that are insufficiently nourished become mortified because they are not capable of exuding, as it were, the products of inflammation—*i. e.*, they can not get rid of them, but are overwhelmed by them, and the part thus mortifying, as seat of decomposition or as an open gateway for the microbes, will naturally bring ruin to the entire organism. But the tissues endowed with great resources—respectively, compensatory arrangements—not only nourish themselves sufficiently in spite of, or rather just because of, the production of an exudate that is expelled from the organism, but in the increased activity of the essential (internal) labor, they possess not only the means of destroying the internal irritation (respectively, to pass the products of inflammation to the surface), but also to liquefy them later on and to absorb them, or to expectorate them by the action of extrabodily labor.

The same conditions obtain in diphtheria. That a patient with diphtheria becomes septic is a sign of insufficient reaction—of weakness—of the tissues, which succumb to the demands of a marked abnormal irritation (respectively, to the internal compression by the copious exudate), thus paving the way for ever-present parasites.

Therefore, according to our experience, we are not able to look upon the septic change as a specific affection—*i. e.*, as the expression of the genuine membrane-developing process of true diphtheria; in any case, the possibility of assuming diphtheria at all diminishes in proportion to the rapidity of the onset, and to the intensity of the phlegmono-gangrenous, or septic, symptoms. The gangrenous, or septic, process, according to our opinion, is merely an abnormal complication of typical diphtheria, a frequent, it is true, and very serious incident of this affection of the mucous membranes, as ery-

sipelas, hospital gangrene, or puerperal sepsis are complications by means of which the simplest wounds, or even *physiological* processes, may become sources of mortality.¹ In other words, every acute disease is fraught with a possibility of an atypical course—*i.e.*, the development of the specific symptoms of reaction does not occur which furnish the typical (classical) clinical picture. The brief action of the definite etiological factor liberates inadequate disturbances of activity, and thus creates dangers which have nothing in common with the original process—just as a small bed sore may lead to a fatal termination in a convalescent from a severe attack of typhoid fever, who, owing to pronounced weakness, continually remains in the dorsal position. The greatest danger in diphtheria—besides the localization of the typical process in the larynx—is the development of the gangrenous-septic process characteristic of the formation of which—with known etiology—is usually the absence or the very deficient development of the typical (pathognomonic) phenomena of the respective process.

Thus here, too, the statement pronounced by me twenty years ago, in an investigation on endocarditis (Eulenburg's

¹ At the risk of being accused of absolutely unscientific views by the *laudatores temporis præsentis*, I am bound to express the opinion that the law of undulation holds good also in wound disease, including those of puerperal origin, and that even the successful achievements of modern surgery, which in part, it is true, depend also upon an improved technics, and upon an appropriate diminution of noxæ (asepsis), are to a certain extent nothing but the expression of this law—*i.e.*, a valley wave of the predisposition to secondary wound disease—like many other successes which we attribute to our presumedly excellent—because coinciding with an improvement of conditions—hygienic and therapeutic measures. It is probable that the physicians of former days also ascribed the extinction of pest and of English sweating fever to their scientifically established influence upon events! The last word has not been spoken even about the value of smallpox inoculation, or about the significance of the undulation of smallpox epidemics, the diminution of which we deem it opportune to attribute solely to vaccination. *Tempus docebit!*

Real Encyclopädie), still holds good: "Altho the inflammatory process on the valves conditions the primary and secondary dangers, still not the endocardial deposits, yes, not even the formation of ulcers, but the development of the general infection constitutes the principal peril to the patient." This general infection will take place if the normal capacity for reaction does not suffice to remove the irritation, or to localization—respectively, if the noxa is excessively strong.

Thus, in our opinion, the hemorrhagic form of smallpox is nothing but a condition brought about by the unfavorable predisposition of the patient, and for which the smallpox toxin forms merely the process of causation, but not the foundation of the symptom picture; and thus, under certain favorable external conditions, typhoid fever will become hunger or war typhus (of a gangrenous or septic character) which naturally, in spite of the numerous petechiæ and hemorrhages, is not identical with specific exanthematic or petechial typhus, but indicates only the most intense forms of the typhoid disturbance of function occurring under especially unfavorable vital conditions—*i.e.*, an organism which is especially predisposed—by tendency and function, or by internal and external conditions of life—is, under the influence of the respective noxa (a very intense or extensive action), at once injured to such an extent that the typical features of the normal clinical picture are obliterated. The specific reactions, or localizations, or characteristic products by which the adequate regulatory endeavors of the body are manifest, are displaced by a disturbance of activity common to many processes which might well be designated as acute insufficiency of the blood-binding function.

Not quite without reason, this view will be looked upon as a revival of the former theory of putrid fever, and I shall thus be open to the suspicion of antediluvian views. But it is actually impossible for me to free myself from the unfashionable view regarding the significance of the genius epidemicus which is manifest not only in the undulations of the morbidity (the change of

isolated affections—respectively, endemics and pandemics), but also in the special intensity and multiplicity of certain deleterious complications which crowd the typical clinical picture entirely into the background. At any rate, my conviction has not arisen from lack of experience or from insufficient knowledge of the literature, for I have observed all the European epidemics of the last thirty years from very extensive material, and I claim to be also sufficiently familiar with the history of medicine to have an opinion of my own regarding these questions—an opinion which need not be wrong because it is in contrast to the modern theory.

V

Résumé

To sum up: We regard septic diphtheria as being due to a constitutional weakness—*i.e.*, to a secondary form of manifestation resulting from the abnormal form of reaction (predisposition) of the affected organism, or perhaps from the extent of the noxa, and in itself having as little to do with the primary cause of the disease as has sepsis with the prick of a pin, which, altho it may lay open the interior of the body, still must not necessarily be the carrier of the respective microbes, or toxins, which can enter through the open gateway on their own account.

We are of the opinion that there is no disease in which the part of personal or regionary (local) predisposition can be studied to better advantage than in septic diphtheria. The determining factors in this instance are

probably, within wide limits, individual and local conditions (respectively, the *genius endemicus and epidemicus*), presumably in the overwhelming majority of cases not to be identified even with a marked intensity of the pathogenic irritation, let alone with a conspicuous activity or virulence of specific microbes, but merely with unfavorable changes of the vital conditions of the organism in the widest sense. These personal relations decide whether an individual organism reacts with the typical whitish-yellow exudate, which has the tendency of descending and of killing by respiratory insufficiency, or with grayish-yellow or brownish-yellow, shreddy, loose exudate which, from the onset associated with fetid odor from the mouth and with glandular swellings, has a tendency of migrating into the posterior nares (putrid fever).

In fact, I can not banish the idea from my mind that the conditions regarding the *locus minoris resistentiæ* are in no way different here than in an ordinary cold. One person acquires a simple rhinitis; another one, pharyngitis, with subsequent rhinitis; a third individual, rhinitis, with subsequent laryngitis.

The participation in throat affections of predisposition—respectively, of the extent of the primary injury or irritation, or of the significance of a special *genius epidemicus*; *i.e.*, of the markedly unfavorable (general or epidemic) change of the vital and functional conditions—is manifest also by the fact that sepsis supervenes only very rarely upon the most simple forms of angina, but frequently upon severe forms of diseases of the throat characterized by a well-developed general affection (abnormally intense reaction) or by an especial intensity of the local disorder, including primarily the typically diphtheritic process. (Scarlatinal angina, deep-seated phlegmonous processes of the throat predispose especially to sepsis, and it is particularly remarkable of the activity of the *genius epidemicus* that so-called septic, gangrenous diphtheria,

occurs much more rarely as an isolated disease than does the typical croupous form.)

Incidentally stated, according to our experience and in spite of all assertions to the contrary, we consider the danger of infection of diphtheria, especially of the septic form, to be extremely slight; for, first, we have observed many cases of isolated affection, and particularly in places in which the quarantine arrangements were not satisfactory; secondly, we have, apart from the exemption of physicians and nurses, never noted an infection of the children and adults in the neighborhood of patients in whom the presence of diphtheria was recognized too late; thirdly, we can not at all look upon the fact that a great many individuals and often many children of one family become affected, either simultaneously or in rapid succession, as a proof of infection from case to case, but merely as an expression of the same causes that are generally active.

Since the new theory of a curative diphtheria serum is based upon the existence of a specific bacillus, and since the proof of the curative action can be rendered only when the remedy proves its efficacy particularly in cases of specific diphtheritic affection (*i. e.*, in cases in which it is assumed that the diphtheria bacillus alone plays its part), then all objections deserve notice, above all, which are qualified to call the justification of these two assumptions in question. Our contention, that the criteria brought forward for the specificity of the bacillus do not suffice, and that there is no such a thing as a specific diphtheria bacillus, but, perhaps, a Löffler bacillus, will, of course, be no reason for the adherents of the opposite opinion to relinquish their views as to the specific relations of a bacillus to diphtheria. But the fact that, according to the above statistic determinations, an action of the specific serum can come into question possibly only in the septic form of diphtheria—respect-

ively, in mixed infections—should cause even enthusiasts and optimists to become startled, to say the least.

The objection is not at all in order that the remedy prevents the development of the septic process, because it aids the organism in the struggle against the true agent of specific diphtheria—hence, hinders, as it were, the hopeless combat along two fronts, in that it takes charge of warding off the main attack.

This condition would be quite gratifying, indeed; but the assumption, like all absolute analogies deduced from test-tube experiments, or from experiments undertaken in animals, is an illusion. For, apart from the fact that the weighty physiological and pathological objections raised in various places to this conception contradicting the conditions of the energetic, have as yet not been refuted, the patient with septic diphtheria does not, as a rule, die because the typically diphtheritic process is excessively intense or extensive, or because the organism has exhausted itself in its successful defense against the latter, but the lethal termination takes place under manifestations which are by no means characteristic of the particular process or etiology, since they constitute the rule also in other severe affections of the throat—*e.g.*, in scarlatinal disorders of the throat.

The very absence of the normal reaction characteristic of the noxa of diphtheria, the non-presence of the typical; superficial, croupous process, demonstrates—unless we prefer to assume another etiological factor, for which supposition there is no reason whatever—that the body in this instance is incapable of developing the natural process of reaction or recovery. The paralyzed or insufficient tissue, owing to an inadequate, not appropriate, local process, not only allows the entrance of

otherwise harmless microbes—the ubiquitous pyogenic agents—which, under regular conditions (*i.e.*, with normal reaction), may possibly be denied to them just by the development of the typical superficial exudate, but it even constitutes them the rulers of the non-functioning tissue. The primary noxa of diphtheria, which we certainly do not attempt to find among the host of microbes, as little as that of pneumonia, plays here simply the part of a mere process of causation, whereas in typical cases it creates the entire form of reaction—*i.e.*, the process in its entire course. It is true, it ushers in a disturbance in the pharynx in diphtheritic sepsis; but, owing to the special predisposition, it moves in an entirely different direction and dimension than in normal reaction, and, therefore, often causes even the collapse of the debilitated organism by intense *general* sepsis—*i.e.*, by an atypical affection.

Therefore, according to my opinion, only the typical development of the (croupous) exudate indicates the normal activity of the tissues—*i.e.*, only under otherwise normal conditions will the noxa of diphtheria liberate a pathological process running a certain course and characterized by the formation of membranes at the surface, which also represents the adequate reaction—*i.e.*, the one which, under average conditions, regulates in an appropriate manner, unless vital parts are for too long a period of time, or too intensely deprived of their functions (laryngeal stenosis). In the other case, owing to a special individual predisposition or in consequence of excessive intensity of the noxa, the activity of the tissues is or becomes paralyzed from the beginning, and, the compensation in the tissues being insufficient, localization does not succeed even by sacrificing of a certain portion of the un nourished parts (formation of pus, ulcers, or partial disintegration of tissue), but a rapidly progressing process of mortification of all layers offers a favorable medium to schiz-

omycetes and facilitates the entrance into healthy tissues (respectively, blood current—*i.e.*, general sepsis).

But whatever theoretical opinion might be cherished, whether our explanations concerning the *fundamental pathogenic difference between typical and septic diphtherias* are accepted or not, the curves shown above should be sufficient to cause the admission that, considering the Curves II and III, there can be no question whatever of an effect of the remedy against specific diphtheria.

But would it not be an incredible accident that the remedy, the inefficacy of which in the specifically diphtheritic process is so drastically illustrated by the above curves, should have been effective just in the septic process (*i.e.*, in those cases in which it was no longer a question of the real toxin of diphtheria), in which, therefore, even the train of thought¹ from which the direct healing potency, the serum, was bound to be created in a particularly complicated manner, will scarcely or not at all come into consideration? We are probably justified in assuming, on the basis of experience and theory—and just the doctrine in vogue to-day can not be in opposition to this conception—that the diphtheria toxin

¹ The enigma of immunization—once apparently so simple and so easily of solution to enthusiasts, which even to-day still appears to be solved to those who are especially easily convinced by experiments and by theories that can be comprehended only with difficulty, in spite of all new complications and possibly for this very reason—this enigma has not come nearer solution, in that attempts were made to prop old errors with new experiments; at least, not to him who, from practical experience and from individual thought, knows the difficulty of the problem—*i.e.*, has comprehended that a solution is never possible on the narrow basis of our present biological knowledge. It would be difficult to uphold to-day any of the former theories which, unfortunately, at once passed into therapeutic practise; and yet the claim of modern humoral pathology of treating patients in a schematic manner—*i.e.*, by force and automatically—is based entirely, except animal experiments, upon such sentiments.

is already destroyed in gangrenous manifestations, that only a septic poison is still active, and thus the statistics of results should entirely eliminate all cases in which the remedy is not employed prophylactically, but is used even in affections with a decidedly gangrenous character—hence, all cases which are severe from the onset. The statistics formerly analyzed by me also showed most conclusively that the influence of the remedy upon *severe* cases from the start on was equal to nothing, and that only the deficiency of many statistics which did not distinguish between severe, medium severe, and mild cases was instrumental in procuring to the serum a renown which properly is due to the benignity of the epidemic. The mortality of the medium severe and of the mild cases—*i. e.*, of those cases which did not present a septic or stenotic character—has never been great at any time, according to our experience—*i. e.*, the severity of an epidemic has always been determined only by the number of such cases as were to be characterized as severe ones from the beginning.

The yearly diphtheria statistics of the Hospital "am Urban," whose inferences, too much in favor of the serum, I was repeatedly compelled to oppose,¹ show, in a most instructive manner, that such a separation can very well be done by experienced physicians, and that it is of the utmost importance. We can but advise every one who disputes the possibility of such a separation to study the above-named statistics, to convince himself that the prognostic determination—respectively, differentiation—of three grades of the disease, as undertaken by Koerte, has stood the test. This has furnished the unobjectionable proof that the mortality of an epidemic is governed exclusively by the number of severe cases. And

¹ Compare Chapters XXIII and XXIV.

yet the serum is credited with successes which it is not entitled to claim on the basis of theory and practise.

The conditions for diphtheria serum—it will be conceivable that I am not able to designate it by the suggestive and fascinating name of “curative serum”—are quite analogous to those which prevailed for Koch’s tuberculin, which, evolved from a theory that, in my opinion, was absolutely incorrect, logically should have been recommended only in the specifically tuberculous process, but never against *phthisical* processes, and, above all, never with the well-known directions as to its employment. This mistake was discovered too late, and then all failures of the remedy were attributed to the existence of a mixed infection, whereas the favorable results were indiscriminately ascribed to tuberculin. This is repeated now, altho in an inverse manner: The “ingeniously conceived” diphtheria remedy fails just in the specific process out of which and for which it has been created; but still, on the one hand, the apparently favorable results—which must be attributed only to the increase of the mild cases, as stated by me and by others years ago—are unhesitatingly (respectively, in consequence of statistical fallacies) credited to the serum, and, on the other hand, successes are claimed even in scarlatinal affections of the throat, whereas the failures are passed over because then it was no longer a question of diphtheria. Such actions, immaterial whether the point in question is tuberculin or diphtheria serum, can be committed only by therapeutists who are determined to have success by all means.

A point which greatly aided diphtheria serum was the fact that it was introduced when coming events had already cast their shadows before—*i.e.*, when the begin-

ning of a distinct valley wave of mortality could already be determined. If the tuberculin of 1891 were first employed to-day when, according to our opinion, an essential decrease of the danger and frequency of tuberculosis already exists, and if only the early cases (hence, also in tuberculosis those that are mild and in part doubtful) were declared fit for treatment—as the orotherapists inject even upon a mere suspicion of diphtheria, and with such cases improve their statistics—therefore, if we again would operate with a curative tuberculin, then for the above-stated reasons, and at the hand of “abortive” statistics, we could again achieve fascinating results—i.e., the long-lasting suggestion which is so very characteristic of hypnotism in the realm of science.

And yet to him who follows the undulations of epidemics the conditions are quite simple also in the domain of diphtheria, since in the natural course of events the deleterious influences usually and luckily change and decrease as spontaneously as—unfortunately—they also develop spontaneously. Any one who closely pursues the history of membranous, or croupous, angina—i.e., diphtheria—can readily reconstruct from the change of the pathological picture—respectively, from the change caused thereby of the *pathogenic conceptions of the authors*—the individual systems of undulation—respectively, the partial waves—which are distinctly recognizable also in the last system of undulation, the acme of which begins at about the end of the seventies. The first to lose its power was the factor which alone is characteristic of diphtheria—namely, the formation of superficial membranes in the regions of the pharynx and larynx; then, after a relatively brief rule, the factor

which weakens the constitution and favors sepsis has also gradually diminished in intensity.¹

The course of diphtheria epidemics, therefore, is not at all different from that of all epidemics—respectively, undulation systems—of acute morbidity, with which personal experience or history has made us acquainted, and even the therapeutic conclusions, according to the dictum “*post hoc, propter hoc*,” repeat themselves. Hesitation prevailed at all times to acknowledge that the causes of the decrease and disappearance of epidemics are unknown, and to recognize that epidemics also are subject to the law dominating nature of development, of coming and passing away. But earnest endeavors prevailed at all times, according to the standpoint of the religious or scientific belief, of the confidence in supernatural powers or in our own, to trace the recurrence of better conditions to divine or human intervention, to miracles, magic remedies, or to the influence of scientific deeds. The measures employed, according to the prevailing standpoint, were and are believingly looked upon as a sufficient and as the sole cause of the success, provided they are applied just at the right time—*i. e.*, at the beginning of a wave valley of the epidemic. Thus, all experiences and considerations now also point to the fact that this favor of the conditions was showered in a full measure upon diphtheria serum, and that the sug-

¹ Even he who does not clinically separate the two forms of diphtheria *qualitatively*—*i. e.*, who disputes the action of a different etiological factor in the septic form, must admit that the same *qualitative* difference at least exists between the croupous and the diphtheritic processes as is present between benign inflammation and suppuration with destruction of tissue, between croupous bronchitis—I do not say fibrinous—and inflammation of the lungs (respectively, pulmonary abscess and gangrene), between acute nephritis, with abundant development of casts and abscess of the kidneys, etc.

gestive addition with which its healing power was emphasized is not justly its due.

The founder of diphtheria-oro-therapy has in most recent times displaced the theory, which resulted in the presumed remedy, by a new one, and thus probably acknowledged that those were right who, like the author, from the beginning combated it as being unfounded. Even if the new theory were more plausible than it appears to us, the abandonment of the first foundation deprives oro-therapy as it existed until now of its *most essential* basis. It is true, to prove that even wrong conclusions result in valuable accomplishments for practise, a celebrated example might be adduced; but then the question is also in order: Does it suffice to promote wrong prepositions to be a Columbus?

Simply because in its time, in the enthusiasm of experimenting, events were considered to be extremely simple and infection disease was identified with injection disease, the belief obtained that all problems were solved by the most simple theory; and, therefore, are we compelled, on the basis of every new fact, to alter the "theory *ad hoc*," whereas, with some criticism, facts long known would have sufficed at once to demonstrate the inadequacy of every one of the modern chemiatrico-humoral theories.

VI

The Clinico-Therapeutic Test of the Serum as Practised So Far Does Not Answer Scientific Requirements

Unfortunately, the recognition of the true relation of matters was for a long period of time impaired or ren-

dered impossible, in that, as customary during the first enthusiasm, the new healing method was inaugurated suddenly, in all places and in all cases. We say "unfortunately" advisedly; for, even in the justifiable endeavor of helping the patient as speedily as possible, the fundamental laws of scientific investigations dare not, after all, be neglected, which are truly of greatest importance in practise, and, therefore, are never left unheeded without subsequent harm.

In order to judge scientifically of the efficacy of new remedies or methods, of the causal connection between remedy and success, it is imperative, above all, to be certain that the conditions under which the application takes place do not *change spontaneously* during the critical period, and, in the main, within a limited period. But naturally, with some knowledge of the law of undulation—*i.e.*, of the inconstancy of all factors of an epidemic—it is impossible ever to guarantee the reliability of these biological foundations with like certainty as can be done in the arrangement of experiments in organic domains; for every one knows that a radical change due to unknown causes occurs often suddenly, and quite as often announced by precursors. If this law—respectively, the signs of the change—were determined as reliably by objective and unbiased series of observations as the manifestations of the pneumonic crisis, an objective investigator should never undertake the test of a new method during the *critical period*. But care should be had under all circumstances not to rate the efficacy of a remedy employed during a critical period too highly. Otherwise it would be necessary to pronounce as justified also the claims of a performer of miracles who practises his hocus-pocus at an opportune time, as is done by the

medicine-men of savage tribes at the time of an eclipse, or who employs a remedy or a magic formula on the fifth day of all cases of inflammation of the lungs, and then ascribes to himself the favorable result which occurs immediately in 90 per cent. of all cases.

We dare not, especially in the face of the signs which already announced the decline of danger of an epidemic (see above), in spite of the really remarkable coincidence of the employment of the serum and the diminution of mortality, look upon the favorable change as being due to a demonstrated success of the serum until thorough endeavors have been made to disprove the objection that a spontaneous improvement had taken place. This would have been surely accomplished if one half of all patients had been treated according to the new, the other half in accordance to the old, method; perhaps in subjecting the even numbers of patients admitted to one, the uneven admissions to the other, mode of treatment. This would have taken all just requirements into proper consideration, and a success of the remedy could have been claimed with full reason if the conditions of recovery in those who were not treated with the serum would have been distinctly more unfavorable than in those treated.

If, in opposition to the hasty action of the orotherapeutists, we proclaim only the method sketched by us as the *only one* that is, at the same time, humane and scientific, objections will naturally be made that then a number of patients would knowingly be excluded from the advantage of the treatment, and thus be condemned to death. This opinion would be correct if at the time we had been dealing with a method that had stood the test beyond all question of doubt—*i. e.*, which had been demonstrated as

efficacious on appropriate material and with all required precautions. But nothing of the kind can be claimed in this instance; for the proof of the curative value of the remedy could, in 1894, be determined only by thorough control examination of the first statements. Enthusiasm and faith in authority may sometimes be justifiable; but imperative, above all, is the greatest caution in the employment of a new remedy which, after all, must not be accepted merely upon trust, and which can not be forced upon all patients of a certain disease group.

The first duty of the physician is to examine the indications and effects carefully, and in some few cases, in order to determine eventual deleterious effects in time, and before they have assumed greater dimensions. Or should we really take the risk, at the order of "science"—*i.e.*, to-day really only upon the recommendations of an experimenter in the laboratory or of an Utopist of theoretical therapy, of utilizing without examination in all cases a remedy that is ineffective or possibly even harmful in itself or in the prescribed form of application, as was the case, for instance, in tuberculin? I wish to recall the fact how the first statements regarding the dose of many otherwise valuable antipyretics, and the recommendation of certain internal and external antiseptics of assumedly no deleterious by-effects, subsequently proved to be erroneous, and that many physicians, and, above all, patients, paid rather dearly for this experience.

It is true, my dutiful conviction—begging pardon for the self-praise—has never permitted me to employ a remedy with "compulsory quotation," which causes the physician to be an automaton. Where is there a trace left of medical activity or responsibility if therapy rep-

resents nothing but some form of automatic reflex upon the name of the disease, and, for instance, at the slightest indication of an inflammation of the throat, the treatment with serum is so automatically given that a layman may *demand* it of his physician, as in times gone by he requested antipyrin in case of fever, or considered the practitioner a quack who would not order a Carlsbad cure in cases of glycuria? If anything may fill me with satisfaction, it is the fact that I never blindly took part in a scientific fashion, and that I adhered strictly to my principle of examining personally and of prescribing according to individuality, even in the ecstasy of tuberculin treatment, which, it is true, I was bound to regard as theoretically unfounded from the very beginning, and as harmful in its magistral—*i. e.*, ordained by its creator—form of application. At that time I administered only minutest doses with the slowest possible increase, and I carefully selected the suitable cases. In this manner I have probably, tho even by negative activity, prolonged or preserved many a life, which otherwise would have rapidly fallen a prey to the intoxication—respectively, to the fever. And just on account of these theoretical views, difficult to be shaken, and of practical experiences, I felt it incumbent upon me at once to proclaim my *a priori* objections to the efficacy of diphtheria serum, and especially to the endeavors of demonstrating its efficacy by suggestion and by unscientific methods. Naturally, among the expedients of such a demonstration the principal part is played by the method which I have called *acute statistics*, and, therefore, I have never missed an opportunity to determine the value of such statistical conclusions by special analysis.

Besides, that not only theoretical faith in the increas-

ing benignity of the epidemic insisted upon restriction of serum treatment—to one-half of the cases—and that really no disastrous consequences occurred to the non-injected, is probably evinced by the fact that the few physicians who had the courage of treating without serum have no worse statistics to show than those who treated with serum.¹

I would, of course, greatly dissuade from throwing the serum treatment overboard to-day, not because I ascribe an even minimal effect to it, but because the steplike rise of the epidemic, which, unfortunately, is again to be expected, would only serve to furnish a new weapon to the ootherapeutists. Indeed, the remarkable fluctuations of the mortality figures at the onset of 1894 were utilized in such a manner as to attribute the decline of mortality to the use of the serum and the reiterated brief upward movement to the non-use of the serum, which, at that time, could not yet be obtained in larger quantities. Hence, I would now advise only to proceed in the manner mentioned above—*i. e.*, in regular turns to inject one patient and to treat the following one without serum. This eliminates all subjectivism in the formation of the material which is to serve as the basis of statistics, and it will be possible, after observations have been made in this manner for a sufficiently long period of time, to make it evident also to skeptics whether or not diphtheria serum has really accomplished what the overwhelming majority of physicians ascribe to it.

¹ Compare, *e. g.*, the former result of Soerensen and the lately reported observations of R. Spohr (Arch. f. physik-diätet. Therapie in der ärztl. Praxis, Oct. und Nov., 1901), which comprise a very limited material, it is true, but, as it appears, very severe cases, and which, besides, were obtained in the same territory as the statistics interesting us here.

XXVI

REMARKS CONCERNING THE PATHOGENESIS OF PULMONARY PHTHISIS

SINCE the time appears to have passed, fortunately, when it was believed possible to ascribe to the positive or negative finding of tubercle bacilli, or, more correctly, of *more or less acid-proof bacilli*, a pathognomonic significance (always denied by me)—the time when the microscopist, away from the sick-bed, was allowed to give directions to the clinician—it follows that the purely clinical features of the pathological picture naturally once more attain an increased significance. Thus I wish, in a clinical interest, once again to call attention to an early symptom of phthisis—described by me quite some time ago,¹ but, to my knowledge, never considered—or, as I would rather say, to an *essential sign of predisposition to phthisis*—namely, to the peculiar odor of the expiratory air of phthisical persons or of those suspected of phthisis, especially younger individuals. This insipid, sweetish, extremely disagreeable odor, which has a distant resemblance to that of putrid bronchitis, and which becomes manifest even at a certain distance from the patient, does not adhere to the sputum, which in a number of cases is present only in minimal quantities, but it appears to be limited to the exhaled air.

¹ O. Rosenbach, "Ueber einen eigenthümlichen Geruch der Expirationsluft von Phthisikern" [On a Peculiar Odor of the Expiratory Air of Phthisical Patients], *Aerztlicher Praktiker*, 1893, No. 22.

This symptom, which I have frequently observed also during the last years, in spite of limited material, is, first, of prognostic significance, in my opinion; for the cases in which I observed it ran a remarkably unfavorable course, altho the other manifestations suggested a more favorable conclusion. Secondly, it is etiologically and pathogenetically interesting as a proof of the cooperation of different factors in the origin and development of processes designated as *phthisical*, but which are not at all identical with *tuberculosis*.

It is singular that the specific odor in the overwhelming majority of cases occurs particularly in by no means well-defined destructive processes of the lungs, and that it is certainly most markedly developed when the physical signs are still insignificant. The odor is absent in infiltration of entire lobes, or in foci which already call forth increased dulness, in cavity formation; I also failed to observe it almost always in cases in which abundant quantities of sputum were in evidence. Since the specific odor does not, or only to the smallest extent, arise in the mouth (respectively, in the pharynx)—hence, owes its origin neither exclusively to an affection of the teeth, of the tonsils, nasal mucous membranes, nor to catarrh of the mucous membrane, so frequently accompanying dyspepsia, the usual cause of fetid breath—its point of origin should be looked for, above all, in the lungs—respectively, in the bronchial system. It may be assumed, with a great deal of probability, that then it is a question of processes of decomposition, which are ushered in and maintained upon the basis of a pathological predisposition—respectively, functional disturbance in the tissues by one or the other form of micro-organisms, in a similar manner as is the case in putrid bronchitis, or gangrene,

or in ozena. The malodorous material produced in the respiratory passages naturally becomes admixed to the expiratory air, and, therefore, can not be demonstrated when the breath is held for some time, nor in the sputum receptacle, whereas every vigorous expiration forces it into the respiratory air, and thus causes it to become manifestly demonstrable.

We have at hand a number of observations, in which nothing but the presence of the conspicuous specific odor gave rise to repeated careful examination of the lungs, which after some time led to the determination of a phthisical affection. We advise, therefore, in cases in which disease of the lungs is suspected, always carefully to control the odor of the expiratory air in all doubtful cases, and, in the presence of the specific odor, to undertake an especially careful examination of the lungs at stated intervals. If the first examination does not shed sufficient light upon the cause and character of the odor (for *fator ex ore* is not rare), because it might possibly be due to decayed teeth or a catarrhal affection of the mucous membrane of the oral cavity, the application of deodorizing mouth gargles and the recommendation of special care of the teeth will be sufficient to set us right within a brief period of time, since these measures cause the disappearance of odor only, the source of which is the mucous membrane of the mouth, but not that which originates in the lungs.

It is surely very remarkable that all persons observed by me had badly decayed teeth, the odor of which was similar, altho not identical, to that of the expiratory air coming from the depths, and it appears plausible to think that a constitutional or local predisposition to phthisis may early become manifest in the nutrition of

the teeth. It is my opinion that individuals with very healthy and strong teeth seem in general to be less predisposed to phthisis.

Since unquestionably a change of views regarding the pathogenetic and pathognomonic importance of the tubercle bacillus is gradually becoming more and more manifest, and since excellent investigators, among whom I desire to name, above all, Hüppe, Martius, Schleich, Riffel, Gottstein, and Nauss, duly recognize the important factors of heredity and individuality, predisposition and constitution, I wish to quote here the concluding sentences of my communication regarding the above-named symptom, as they appear to cast the right light upon the quintessence of the then prevailing views opposed by me:

“Little as we are inclined, on the basis of clinical experience and bacteriological investigation, to attribute to the tubercle bacillus a primary or determining part in the origin of the majority of cases of phthisical processes of the lungs, as much do we support the view that the ordinary pyogenic organism participates, in a great measure, in the causation and maintenance of phthisical processes, in that, either alone or in consequence of their symbiotic relations to the tubercle bacillus, they shape the principal clinical course of the disease and the final picture of the tissue disturbance. It is essential, therefore, that their colonization in the cavity of the mouth must be most energetically prevented by the extermination of even the smallest foci and colonies in the tissue; for they furnish the soil for the further processes of destruction. Naturally, this is not meant to imply that the mucous membrane of the mouth should, in every suspected case, be maltreated with

strong disinfectants, but it is intended merely to suggest that the modern achievements of hygiene and therapy of the mouth and of the teeth should be rationally utilized in such a manner as they deserve to be.

“If unquestionably, in the struggle against pulmonary phthisis, hygiene which strives for a strengthening of the constitution stands in the foreground, then that part of hygiene must be particularly promoted which aims at the rational care of the mouth and at the removal of all deleterious influences which endanger the safety of this portal of entrance, and which tends to prevent as much as possible the colonization of pyogenic bacteria, their *accommodation to the organism*, and the danger of their entrance into a weak lung resulting from this accommodation. Since our observations—once our attention had been called to the relations of an affection of the cavity of the mouth to inflammatory disorders of the respiratory passages—have shown us, in an ever-rising measure, how often the results of deficient care are found in the very individuals who are afflicted with chronic diseases of the lungs, the duty became incumbent upon us not only to make the lungs of the healthy or of those already affected an object of hygienic or therapeutic measures, but to apply the same care in all cases also to the organs of the mouth.”

Hence, not the tubercle bacillus should be combated, but the deficiently functuating part of the general activity must be removed which creates the predisposition to endoparasitism—*i.e.*, as I have repeatedly explained, which furnishes to the otherwise benign parasites the opportunity for abnormal proliferation and for the entrance into the tissues, rendering them pathogenic factors which, however, must not necessarily be identical

with specific generators—*i. e.*, with specimens of a certain species.

Especially significant of the one-sidedness of bacteriological methods of consideration is the readiness with which they have disregarded the fact, *e. g.*, that, in spite of insufficient care of the mouth, tuberculous affections of the mouth are extremely rare in phthisical patients; that likewise, in affected gums and in high grades of catarrh of the mouth, pharynx, or nose, various forms of ulcerative processes are found, it is true, but only rarely tuberculous ones; and that, finally, the interior of the nose in adults—even in cases of lupus—is not very often the seat of tuberculous affections. Stomach digestion, by the effect of which it was believed that the rarity of the occurrence of primary infection of the intestine could best be explained, does not come into consideration for the above regions, and that saliva does not protect is demonstrated, above all, by the frequent localization of pathological ulcerations on the epiglottis and in the most superior portion of the posterior wall of the larynx, which surely comes in contact with saliva. It is very singular, indeed, that the very parts through which alone the introduction of the assumedly specific, acid-proof bacillus may take place, are greatly immune to tuberculosis, whereas they present the most favorable soil imaginable to suppurative processes—respectively, to inflammation and ulceration. This is best calculated to prove the importance of predisposition, and it teaches that a destruction of tissue does not take place because some microbe is present, but that the microbes enter the tissues only in such cases in which conditions are at hand, due to a natural tendency or to an external influence, favoring a disturbance of the internal functions—

i.e., an insufficient production to preserve the existence of the tissue. I do not mean to deny that such an external factor may occasionally consist in an especially marked actuation (so-called virulence) of otherwise harmless (symbiotic) microbes; but this fact must first be proven, which is not easy, since the influences which cause an actuation of the microbes may as readily have brought about a reciprocal impairment of the resisting power of the tissues of the respective host.

It is true, at present a period begins which inaugurates a change in this matter also—*i.e.*, ever widening circles commence, just in the domain of the etiology of phthisis, to look upon predisposition and heredity no longer as negligible quantity. According to infallible experiences, we shall soon again have a telling proof of how rapidly the world forgets, not only facts, but, very particularly, scientific errors not pleasant to remember. The “always wise” are already at work to show that, after all, neither in the realm of surgery nor in that of internal medicine any one really ever had considered microbes the all-sufficient—let alone, the sole—cause of diseases, and had ever denied the essential importance of heredity, of the *genius epidemicus*, and of individual predisposition.¹ *Sooner or later it will be shown to the indefatigable combatants against the encroachments and errors of orthodox bacteriology—with the same emphasis as they were formerly accused of unscientific views—that they have wasted their strength in a fight against windmills.*

¹ The constitution is only one, the important, element of predisposition—respectively, of the form of reaction; *i.e.*, the manner of the function is influenced by the constitution, it is true, but it is to a great measure dependent upon external factors. Hence, functional nosology is not identical with constitutional pathology.



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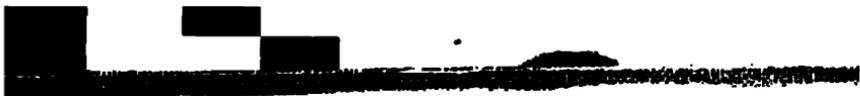
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